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THE FRACTIONATION OF THE YTTRIUM EARTHS BY MEANS OF THE SUCCINATES

BY

RAYMOND C. BENNER
Assistant Professor of Chemistry
University of Arizona

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
THE UNIVERSITY OF WISCONSIN
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THE FRACTIONATION OF THE YTTRIUM EARTHS BY MEANS OF THE SUCCINATES

INTRODUCTION

The separation of the rare earths is, at the present time, as it has been since their discovery, one of the most difficult problems of chemistry.

The various methods of separation may be roughly divided into four classes,

(1) Separation by oxidation
(2) Fractional crystallization
(3) Separation dependent upon their physical properties
(4) Fractional precipitation.

The separation by oxidation depends upon the property which some elements possess, of forming higher oxides, and can be carried out:

(a) By oxidation in the dry way, either by heating in contact with the air or by means of fusion or ignition with some oxidizing reagent.

(b) By oxidation in the wet way, with such reagents as hydrogen peroxide, chlorine, or ammonium persulphate.

One of the cheapest, as well as most effective methods of separation is fractional crystallization. In many cases the separation is greatly aided by the addition of some compound with which the rare earths will form a double salt. These double salts frequently crystallize much better than the simple salts and greatly aid in the separation. Both organic and inorganic salts have been utilized, and crystallization has been effected from water, acids, and inorganic solvents.

The separations by physical means have been but little employed and have met with but little success. They comprise methods such as the distillation of the chloride and of the metals themselves.

Fractional precipitation is of interest because of the behavior of various organic acids and their salts when used as reagents for the separation of the yttrium earths. In the search for reagents which will precipitate any one or more of the rare earths from a mixture of the same, types of practically all the different groups of chemical compounds have been tried. Among these, the organic acids or their alkaline salts present great interest when considered from the standpoint of their applicability to these separations.

The alkaline succinates are of special interest because the time of formation of the insoluble earth succinate resulting from their addition to a solution of yttrium earths, is so greatly delayed that it is possible for equilibrium to be more readily established than when the precipitate is formed instantaneously. Moreover, the physical condition of the precipitate is of such a character that it can be readily handled.

HISTORICAL

The succinates have been proposed as analytical reagents from time to time, and have been employed as a means of separating the rare earths from the more common elements.[1] Since the advent of the oxalate method, we have had a cheap and unexcelled method for the separation of the rare earths from associated elements, so that, in this connection, the succinates are of but historical interest.

A few of the rare earths succinates have been made and analyzed; but they never have been utilized as a means of separating the earths of the yttrium group.

In order to test the applicability of the succinates as reagents in the yttrium group, the yttrium earths were extracted from a number of rare earth minerals of widely different character.

TREATMENT OF SAMARSKITE

Fifteen pounds of Samarskite containing very little gangue mineral, was treated with concentrated hydrofluoric acid, according to the method of J. L. Smith. The mineral dissolved with effervescence. The columbium and tantalum passed into solution while the earths remained as insoluble fluorides. These insoluble fluorides were washed thoroughly with water by decantation, after which they were dried and treated with concentrated sulphuric acid. After a copious evolution of hydrofluoric acid fumes, the mass was warmed and finally heated until heavy fumes of sulphuric acid were evolved. The pasty mass was allowed to cool, when it was extracted with water and the insoluble residue which consisted, more or less, of the oxides of columbium and tantalum, insoluble sulphates and a little of the undecomposed mineral, was thoroughly washed with water by decantation. The sulphate solution of the earths and uranium was neutralized with sodium hydroxide. Oxalic acid was added and the oxalates precipitated. These crude oxalates were then ignited, dissolved in nitric acid and treated with a saturated solution of potassium sulphate with the addition of solid salt. The soluble yttrium double sulphate solution was precipitated with oxalic acid, the precipitate ignited and dissolved in nitric acid, which solution was again treated with potassium sulphate in the same manner. Three such treatments with potassium sulphate in the acid solution were found necessary to remove the insoluble earths and, after these treatments, the didymiums could not be detected in a strong solution of the nitrates by means of their characteristic absorption spectrum, nor could cerium be detected by means of hydrogen peroxide.

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[1] Böhm, *Seltene Erden.*

FRACTIONATION OF THE OXIDES

About one hundred grams of the oxides were dissolved in nitric acid, the excess of acid neutralized with ammonia, and the solution diluted to a liter. Four hundred cubic centimeters of a saturated solution of sodium succinate were added to the boiling solution, in portions of 100 cc at a time, and the boiling continued for about five miuutes. After the addition of the last portion the precipitate was filtered off and washed with 400 cc of hot water. On cooling, another precipitate formed, which remained insoluble even when boiled. It was filtered off and combined with the main portion. The filtrate was again boiled and allowed to cool but no precipitation occurred. Fractionation was continued by addition of the succinate solution in the same way, until all of the rare earths in solution were precipitated, making twelve different fractions.

SERIES I

The atomic weight of each fraction was determined by the oxalate method, and a gram of oxide from each was dissolved in nitric acid, evaporated to a syrup, taken up in five cc of water, and the absorption spectrum measured through a layer $\frac{1}{16}$ inch thick.

FIRST SERIES.

Number.	Wt. of fraction in grams.	Atomic weight.
1	22.2	114.2
2	15.8	111.83
3	10.0	110.06
4	8.8	111.3
5	9.0	108.5
6	7.1	107.2
7	7.0	105.6
8	6.1	104.4
9	7.0	101.0
10	6.4	97.0
11	4.0	95.8
12	3.0	......

SERIES II

In starting the second series, those fractions of similar color and of nearly the same atomic weight were combined, dissolved in nitric acid, evaporated to a thick syrup, taken up in water, and the succinates precipitated at a boiling temperature by the addition of sodium succinate solution, filtered and washed as before. This was carried on until there was no further precipitation on the addition of sodium succinate. Atomic weights and spectroscopic readings were taken in the usual manner.

By this method of fractionation, the earths having the heaviest atomic weights are precipitated first, which showed that the succinates of the earths having the lighter atomic weights were the most soluble under these conditions.

FRACTIONS IN SERIES II

A	130 116 104
B	123 ... 115 98.5
C	114 108 99.7 ...
D	104 97 ... ...

In the first series there was a gradual decrease in atomic weight of the fractions, the color of the oxides became lighter and all the lines of the absorption spectrum dimmer, until in fraction 11 they were quite indistinct and showed an approach to pure yttrium. In series II, it will be noted that in four portions of series I which were taken, a much sharper separation is obtained than in series I. A and B, consisting of earths of higher atomic weights, show a greater separation than do C and D, although in all four portions much greater differences appear in the character of the fractions than in series I. In all cases the color of the oxides and the strength of the lines in the absorption spectrum vary in the same ratio as do the atomic weights. All three of these factors show us that erbium and other earths of heavy atomic weight concentrate in the first fractions, while yttrium concentrates in the last.

Series 3 and 4 show nothing which is not demonstrated by 2, but give further proof of the same points.

The oxide having the lightest color (being nearly white) is also the lowest in atomic weight—93, and has practically no absorption spectrum. It may therefore be considered as nearly pure yttrium, mixed with small amounts of samarium, europium, and holmium. On the other hand the oxide having the darkest color has an atomic weight of 139 and is a mixture of the heavier earths erbium, holmium, terbium, samarium, and europium with a little yttrium.

FACTORS INFLUENCING THE EFFICIENCY OF THE SEPARATION

Because of the results thus far obtained, and the ease with which the fractionation developed, the following factors were studied:

1. The effect of fractionation in dilute solution as compared with the same operation in a strong solution, the strength of the succinate solution being varied as well as that of the earths.
2. The value of sodium succinate as a reagent for fractionation as compared with ammonium succinate.
3. The sudden addition of the succinate as compared with the addition drop by drop.
4. The effect of stirring on the precipitation.
5. The addition of various substances to the solutions.

In order that the influence of these factors might be verified by experiment, several hundred grams of the yttrium earth oxides were prepared from monazite and treated with potassium sulphate until there was not more than a trace of didymium present. They were then precipitated with oxalic acid and ignited. The oxides were dissolved in nitric acid, evaporated to a syrup and taken up with water. A solution neutral to methyl orange was then obtained and its strength determined.

A solution of sodium succinate was made by adding sodium hydroxide to succinic acid until it was neutral to phenolphthalein, and the strength of this solution was determined. An ammonium succinate solution of equal strength was prepared by the addition of ammonia to succinic acid until it was neutral to litmus.

Sixty cc of the yttrium nitrate solution, containing seven and eighty-four hundredths gm. of the rare earth oxide, were diluted to one liter and fractionated in various ways so that six fractions were obtained in each case. The following experiments were made by the addition of equivalent amounts of the precipitating reagent for each fraction precipitated.

Experiment 1. was made by the addition of fifty cc of sodium succinate for each fraction, all the succinate being added at once.

Experiment 2. was a duplicate of the first, except that the succinate was added drop by drop.

Experiment 3. The alkaline succinate was added to the yttrium earths in the presence of sodium acetate.

Experiment 4. Sodium nitrate was added to the solution in such quantity that the solution contained five per cent of the salt, after which the succinate was added.

Experiment 5. The volume was reduced from one liter to five hundred cc.

A second series of experiments was conducted under similar conditions with ammonium succinate replacing the sodium succinate and with ammonium acetate and nitrate replacing the sodium salts. The various experiments described led to the conclusions: The separation can be most satisfactorily made when the precipitating reagent is added drop by drop. Sodium succinate is slightly superior to ammonium succinate as a precipitating reagent. The fractionation is not aided by the addition of sodium acetate or nitrate to the solution of the yttrium earths, when sodium succinate is used, nor by the addition of ammonium acetate or nitrate when ammonium succinate is the precipitating reagent.

BEHAVIOR OF SODIUM SUCCINATE TOWARD DIFFERENT MIXTURES OF THE RARE EARTHS

It is well known that different mixtures of the rare earths conduct themselves differently when treated with the same reagent. With one mixture a certain reagent may give a very good separation, while with another, which contains the same earths in a different proportion, the separation may be unsatisfactory.

It seemed advisable to make a trial of this separation on various minerals from different localities and upon mixtures having different chemical composition. It was therefore thought best to apply the succinates to the separation of a mixture of earths containing a large percentage of the cerium group. The earths from monazite were employed.

Fractionation of Earths Containing Both Groups

The oxalates of the rare earths from monazite were ignited to oxides, taken up in nitric acid, evaporated to a thick syrup, and the syrup dissolved in water. The cerium was reduced to the cerous state with hydrogen peroxide, excess of which was removed by boiling the solution. 61.6 grams of these oxides in the form of the neutral nitrates, were diluted to 1000 cc and fractionally precipitated by means of a solution of sodium succinate containing 200 grams per liter, 100 cc of the solution being added at a time. The fractions, after being ignited to the oxide, were of a similar dark brown shade, except the last two, which were a little lighter in color. The atomic weights were:

No. 1	At. Wt. 149.5	No. 6	At. Wt. 146.0
2	147.0	7	143.0
3	147.0	8	143.0
4	150.0	9	143.0
5	149.0		

The atomic weights show that there is very little separation of the elements of lower atomic weight from those of higher, and therefore little or no separation of the cerium from the yttrium earths. The different fractions compared as to absorption spectra were alike, except the two extremes. Fraction No. 9 seemed to give a little fainter spectrum than the others. The color of the oxides was the same, the characteristic dark brown of ignited oxides of the cerium group, except that of the last fraction. This had a little lighter color, showing that there was a slight separation at this point.

As there had been scarcely any separation when the earths contained a large per cent of the cerium group, the method was tried on different mixtures of the yttrium earths from various minerals. To obtain mixtures containing yttrium earths in varying proportions, different minerals from several localities, were taken and the yttrium earths extracted and fractionated by this method. These minerals were xenotime, gadolinite from Langesundfiord, Norway, fergusonite from Gaalenerene, Norway, euxenite from Arendal, Norway, keilhauite from Tvedestrand, Norway, and a sample of gadolinite from Texas.

XENOTIME

95 grams of the mineral, ground to pass 100 mesh, were thrown, small amounts at a time, into fused ammonium hydrogen sulphate. The greenish mass was extracted with cold water containing a little hydrochloric acid. This extraction was continued until ammonia no longer gave a precipitate in the wash water. The solution was decanted and ammonia added to neutralize the excess of free acid. It was then treated with potassium sulphate in excess, the resulting soluble double sulphate solution treated with oxalic acid, and the oxalates converted by ignition into oxides. These were then taken up with nitric acid, evaporated to a syrup, which converted them into neutral nitrates, and dissolved in a liter of water. 6.83 grams of oxide were then fractionated with sodium succinate solution in the same way as was fergusonite, with the exception that 12½ cc of succinate solution was added at a time.

From a comparison of the atomic weights of the different fractions (112.5, 109.4, 105.7, 101.6, 98.5 in order of precipitation), the color of the ignited oxides and the spectroscopic readings, which grew fainter and fainter with each succeeding fraction, it was established that the elements with higher atomic weights were concentrated in the first fractions, while the yttrium, having no absorption spectrum, the lightest atomic weight and a white oxide, accumulated in the mother liquor. This follows, in all respects, the observations made on the yttrium earths from samarskite.

GADOLINITE FROM LANGESUNDFIORD, NORWAY

95 grams of the gadolinite were pulverized, moistened with water and treated with aqua regia, until the residue was colorless. The solution was evaporated to dryness to dehydrate the silica, and then taken up in water. After filtering, ammonium oxalate was added as long as a precipitate resulted. The oxalates were converted into the oxides by ignition, dissolved in the smallest possible amount of hydrochloric acid, treated with an excess of potassium sulphate in the cold. and the insoluble potassium

double sulphates washed with a cold saturated solution of potassium sulphate. The earths forming soluble double sulphates were precipitated with oxalic acid, and converted to the oxides by ignition. The 25 grams of oxide obtained, were changed to the neutral nitrates, diluted to a liter and fractionated by the addition of 40 cc of a 5 per cent solution of sodium succinate for each fraction. The amount in each fraction was determined by weighing the oxide.

The yttrium earths from this sample of gadolinite are in all respects, similar to those from xenotime, as concerns their behavior toward sodium succinate. The color of the oxides, atomic weight of the fraction (in order of precipitation 113.8. 109.9, 108.0, 107.2, 105.6, 103.2, 98.1, 98.1) and the observations of the absorption spectra were found to be practically identical, except for the more gradual change in these earths, which is to be expected from the greater number of fractions.

FERGUSONITE FROM GAALENERNE, NORWAY

105 grams of this specimen were ground to a fine powder and fused with 400 grams of potassium acid sulphate. The fusion was pulverized and taken up with water. The solution was decanted and the residue washed with cold water until the wash water gave no precipitate with ammonia. The solution was then made alkaline with ammonia, and the precipitate filtered off and washed until the wash water was no longer alkaline. The precipitate was dissolved in nitric acid and the solution heated for several days, water being added occasionally to replace that lost by evaporation. The precipitated metallic acids were filtered off and washed; the filtrate was neutralized with ammonia and the rare earths precipitated with oxalic acid, filtered, washed, and ignited. The oxides were dissolved in hydrochloric acid, evaporated to a syrup, dissolved in water, and treated with potassium sulphate. From the solution of the soluble double sulphates the earths free from didymium were precipitated with oxalic acid, converted into oxides, dissolved in nitric acid, and evaporated to a syrup. The oxides, weighing 10.85 grams, were transformed into nitrates, the solution made neutral to methyl orange. diluted to a liter, and fractionated by the addition of 25 cc of a sodium succinate solution for each fraction.

In this case, the sodium succinate was added drop by drop, the solution being kept at a boiling temperature and constantly stirred with a mechanical stirrer. Each fraction was filtered off as it was precipitated, and the filtrate treated as before, the volume of the solution being kept at a liter all the time. The precipitated succinates were ignited to oxides, taken up with nitric acid, evaporated to a syrup, dissolved in water and examined with the spectroscope. The neutral solution, which was very slightly acid before examination with the spectroscope, was diluted to 800 cc, precipitated with oxalic acid at a boiling temperature, filtered on a weighed filter, washed, dried, and the weight of the oxalate determined. From this the weight of the fraction was calculated.

This series of fractions is of more interest than any of the preceding as the mixture is more complex and of lighter atomic weight. The separation is somewhat sharper, as is shown by the disappearance of some of the lines from fraction No. 4. The oxides also vary more in color, than in any of the preceding cases. The atomic weights vary thus,—115.4, 112.4, 110.5, 102.5 in order of precipitation.

EUXENITE FROM ARENDAL, NORWAY

300 grams of finely pulverized euxenite were treated with hydrofluoric acid in a large lead dish until there was no more action. The insoluble fluorides were washed with water, and acidified with hydrofluoric acid until most of the soluble fluorides were extracted. The insoluble fluorides were converted into sulphates by heating with concentrated sulphuric acid. The excess of sulphuric acid was driven off and the pulverized sulphates taken up with ice-water. This solution was treated with potassium sulphate, the soluble sulphates treated with oxalic acid, and the oxalates converted into oxides by heat and taken up in nitric acid. The treatment with potassium sulphate, and precipitation with oxalic acid were continued until the soluble double sulphates were free from didymium. The oxides were dissolved in nitric acid, evaporated to a syrup, diluted with water to a liter, heated to boiling and fractionated in the neutral solution by adding sodium succinate.

The yttrium earths from euxenite can be considered as identical with those of fergusonite, as far as their conduct toward sodium succinate is related. The atomic weights were, 115.5, 112.7, 110.0, 108.2, 104.5, 102.5 in order of precipitation.

Gadolinite from Texas

About 300 grams of finely pulverized gadolinite were treated with boiling hydrofluoric acid in a lead dish, for several hours. The insoluble fluorides were washed with water containing hydrofluoric acid and converted into sulphates. The sulphates, after having been heated to drive off the excess of acid, were pulverized, and dissolved in ice water. The solution of the sulphates was saturated with potassium sulphate, the insoluble sulphates filtered off and the soluble sulphate solution treated with oxalic acid. The alternate treatment with potassium sulphate and precipitation with oxalic acid were continued until the solution was practically free from the didymiums. The oxides, amounting to 27 grams, were dissolved in nitric acid, evaporated to a syrup, dissolved in water, and diluted to a liter. The solution was made neutral with ammonia, and the earths fractionated by means of sodium succinate.

The earths from this sample of gadolinite may be considered as similar to those from euxenite and fergusonite. The atomic weights (122, 117, 112, 112, 108.5, 103, 102.5 in order of precipitation), and the spectroscopic examination show a gradation similar to that in the case of the other two minerals.

Keilhauite from Tvedestrand, Norway

About 1500 grams of finely pulverized mineral were treated with hydrofluoric acid and kept at boiling temperature for three hours. The insoluble fluorides, after being washed several times with water containing this acid, were converted into sulphates by heating with concentrated sulphuric acid, the excess of acid was driven off and the sulphates ground to a fine powder and taken up with ice water. The solution was precipitated with oxalic acid, and the oxalates converted into oxides, which were taken up in nitric acid and treated with potassium sulphate. The two processes were alternately repeated until the soluble double sulphates showed only a trace of didymium when examined by the spectroscope.

17 grams of the rare earth oxides thus obtained were dissolved in nitric acid, evaporated to a syrup, taken up with water, the solution diluted to a liter, neutralized with ammonia and the earths fractionated by ammonium succinate.

The earths from keilhauite are a little lighter in atomic weight (116.5, 116.5, 108, 104, 104 in order of precipitation) than those from fergusonite, and show a somewhat sharper separation, but in other respects are the same.

DEPORTMENT OF THE SUCCINATES OF THE ERBIUM EARTHS

The study of the above minerals has shown that sodium succinate is uniform in its action toward different mixtures of rare earths having low atomic weights. The separation seems to be more marked as the average atomic weight of the mixture becomes greater, or as the percentage of the earths having heavy atomic weights increases. In order to experimentally investigate this, sodium succinate was used as a fractionating agent on mixtures with higher atomic weights.

ERBIUM EARTHS FROM MONAZITE

A large quantity of oxalates from monazite was ignited to oxides, and taken up in nitric acid, the calculated amount of $Mg(NO_3)_2$ added, and the solution allowed to crystallize, until magnesium nitrate separated out. The mother liquor was treated with potassium sulphate, and the soluble double sulphates precipitated with oxalic acid, washed, dried and ignited to oxides. These were fractionally precipitated with potassium chromate and 9.4 grams of a mixture of oxides having an atomic weight of 148.5 were obtained. These were converted into the neutral nitrates, diluted to a liter and fractionated at boiling temperature by adding ammonium succinate, drop by drop.

The atomic weights in order of precipitation were,—152.5, 154, 148.5, 139, 124.

ERBIUM EARTHS FROM SAMARSKITE

9 grams of oxides from the fractionation of samarskite by the succinate method, having an atomic weight of 122.5, were converted into the neutral nitrates, diluted to a liter, and fractionated by adding sodium succinate drop by drop.

The atomic weights in order of precipitation were,—133, 134, 131, 127, 122.5, 112.5, 103. The color of the oxide varied from brown to nearly pure white.

From a study of the fractionation of mixtures of the yttrium group having heavy atomic weights, it is seen that these are separated by fewer fractionations than those mixtures having lower atomic weights, and in a much sharper manner. The method is consequently best suited for earths having heavy atomic weights.

COMPOSITION OF YTTRIUM SUCCINATE

A few of the rare earth succinates have been analyzed: Czudnowicz and Cleve (Bull. Soc. Chim. Paris 21, 202) report the succinate of lanthanum as $La_2(C_4H_4O_4)_3.5H_2O$.; Cleve (ibid. 43, 172) reports that of samarium $Sm_2(C_4H_4O_4)_3.3H_2O$ (without analysis) also that of yttrium (with analysis) as $Yt^2(C_4H_4O_4)_3.3H_2O$ (*ibid* 18, 296), and (with analysis) that of erbium as $Er_2(C_4H_4O_4)_3 \frac{1}{2}H_2O$. Czudnowitz (Jahresbericht, 1861, 189) tells how to prepare the succinate of cerium, and gives some of its properties. $Ce(C_4H_4O_4).1\frac{1}{2}H_2O$, cerous succinate, is reported by him. Recently Sir Wm. Crookes made a succinate of scandium to which he gave the formula, $Sc_2(C_4H_4O_4)OH.H_2O$.

PREPARATION OF YTTRIA

Mixed residues containing the yttrium earths from various sources, and giving only a trace of the didymium lines, when observed in a concentrated solution of the nitrates, and no evidence of cerium when tested by hydrogen peroxide, were selected. These were obtained in the form of oxides by the ignition of the oxalates. They were dissolved in nitric acid, concentrated until the nitrates just began to decompose, and then dissolved in water. The neutral solution of the nitrates was slowly poured into a saturated solution of potassium sulphate and more solid potassium sulphate added. This was allowed to stand for a week with occasional stirring, when the soluble double sulphates were filtered off, and the earths precipitated with oxalic acid and ignited to the oxides. 150 grams of the oxides were rubbed in a mortar with chromic acid (four parts of the oxide to nine of the chromic acid) and the chromates of the yttrium earths thus formed dissolved in 15 liters of water. This solution was then transferred to a large vessel, in which it was heated to boiling and potassium chromate solution added drop by drop, with constant stirring. Nine fractions were made in this manner, and the ninth gave only the faintest trace of an absorption spectrum, when observed through a saturated solution of the nitrates ¾ inch thick. The last fraction was converted into chloride by boiling the hydrochloric acid solution of the chromates with alcohol. This reduced the chromates to chlorides and from this slightly acid solution the yttrium earths were precipitated with oxalic acid, converted by ignition into oxides and then to neutral nitrates by the ordinary method. The atomic weight of the yttrium was 90.1.

The neutral nitrate of yttrium obtained in the foregoing manner was precipitated in a dilute solution at boiling temperature by adding sodium succinate drop by drop, with constant stirring. The precipitate was filtered off, washed with boiling water, and dried over sulphuric acid, until the weight was constant. The crystalline compound prepared in this manner, was white. The analysis showed it to be a normal succinate.

Theoretical for $Yt_2(C_4H_4O_4)_3.2\frac{1}{2}H_2O_2$ Yt=90.1.

	Theoretical.	Found.	
Yt	31.40	31.89	31.79
C	25.12	25.83	25.45
H	3.00	3.28	3.30

SOLUBILITY OF YTTRIUM SUCCINATE

The salt was introduced into a flask of resistance glass connected with a reflex condenser, boiled for seven hours and filtered while hot. One liter, when evaporated to dryness in a platinum dish, gave 0.054 grams of oxide, equivalent to 0.131 grams of yttrium succinate.

The same experiment was repeated, the boiling being continued for three days of seven hours each. The result was 0.0618 grams of yttrium oxide equivalent to 0.1475 grams of the succinate.

SUMMARY

1. The succinate fractionation can be carried on with great ease as precipitation takes place slowly. The precipitate is easy to handle and wash, and is one which can be prepared for the next fractionation without difficulty merely by ignition to the oxide and taking up in nitric acid.

2. The best separation can be most efficaciously performed by treating a neutral boiling solution of the nitrates with sodium succinate, added drop by drop. It makes very little difference whether the solution is stirred or not. As long as the concentration of the yttrium earths does not exceed 2 or 3 per cent the separation is satisfactory.

3. The yttrium earths from xenotime, fergusonite, euxenite, keilhauite and two samples of gadolinite as well as from two samples of higher atomic weight from monazite and samarskite have been experimented with, and it has been found that the action of the alkaline succinates upon these different mixtures of the yttrium earths is quite uniform and that the best separation is given when there are about equal amounts of the erbium earths present with the yttrium earths. When used on the mixed cerium and yttrium earths it is without value.

4. Finally yttrium forms a normal succinate having the formula $Yt_2(C_4H_4O_4)_3.2\frac{1}{2}H_2O$. It is a white salt, of which 0.1392 grams are soluble in one liter of water.

APPENDIX

IMPORTANT SPECTRUM LINES

Arranged from article by R. J. Meyer in Abegg's Handbuch der Anorganische Chemie Vol. II-I

Nd	Pr	Er	Tb	Sm	Eu	
				362		
				375		
					(380.5)	
					(385.5)	
				390		
					395	400
				402		
				407		
				417		
420						
428						
429.4						
435.1						
	(441–443)			443		
	444–445					
		447.5–451.5				
				(453)		
462.4				463		
					465	
469.1	469					
476.8				476		
	481					
		486.5–487.7				
			488			
		490.5–491				
				498		500
510.9						
		518 -522.5				
522 (—)		522.5–523.5			525	
				529		
532					535	
		540 –541.5				
				559		
		(570—)				
578.3 (—)						
	589 or 590				590	
629.2	595 or 596					600
637.3						
		647.5–651.5				
		651.6–654.5				
		668				
673.1						
680.4						
691						
732.4						

(—) = center of band. Lines underlined, most important.
Faint lines, ( ).

A similar table containing all the lines of the rare earths is given on page 107 of the book, Spektroskopie und Kolorimetrie, by Emil Baur.

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THE SEPARATION OF THE GADOLINIUM EARTHS AS STEARATES

BY

CHARLES WARREN HILL

Instructor in Chemistry, The University of Wisconsin

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
THE UNIVERSITY OF WISCONSIN
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INTRODUCTION

The resemblance of the gadolinium earths in chemical properties to the cerium earths on one hand and to the yttrium earths on the other renders their separation doubly difficult. On account of the mutual similarity of these earths, their isolation is one of the most unsatisfactory in rare earth work. An efficient and rapid method for the isolation of these elements is therefore of interest and importance.

The aim of the present work is the application of the separation as stearates to the earths of higher atomic weight in general and more specifically to the gadolinium earths, gadolinium, europium and samarium.

THE SEPARATION OF THE GADOLINIUM EARTHS AS STEARATES

THE STEARATE SEPARATION

Separation of rare earth mixtures as stearates is accomplished by the addition drop by drop of a hot alcoholic solution of potassium stearate to a dilute neutral solution of the earth nitrates, in quantity sufficient for the precipitation of only a fractional portion of the earths present. The earth solution is thoroughly stirred during precipitation which begins at once with the first few drops of the stearate solution. The precipitate is curdy and lighter than water.

Better separation is effected by prolonged mechanical stirring or beating of the mixture, resulting in the formation of a fine granular precipitate which may be separated from the solution in a Büchner funnel.

The last fraction of a series is best precipitated as oxalate from the hot solution, since the excess of potassium stearate forms a slimy precipitate which it is difficult to separate from the solution.

The potassium stearate solution is prepared by dissolving 300 grams of stearic acid in a liter of alcohol, neutralizing with a solution of potassium hydroxide using phenolphthalein as indicator and diluting with water to two liters. 50 cc of such solution will precipitate a quantity of the earth stearate yielding about two grams of the oxide on ignition.

The influence of stirring was shown experimentally by precipitating fractionally a mixture of earths, the average atomic weight of which was 126. The atomic weight of the first fraction which was not stirred after precipitation was 127, while the atomic weight of the same fraction after rapid stirring for 48 hours was 135.

SEPARATION OF RARE EARTHS FROM MONAZITE

The rare earths obtained from monazite as oxalates, ignited and converted into nitrates, were fractionally crystallized from the nitrate solution as the double magnesium nitrates, crystallization being continued until magnesium nitrate separated out. The crystallized part contained the major portion of the cerium, lanthanum and the didymiums. From the remaining solution three large fractions of insoluble double potassium sulphates were crystallized. The earths remaining in solution were treated as described on page 10.

Insoluble Double Sulphate Portion

The earths in the last insoluble double sulphate fraction were converted into hydroxides by boiling with sodium hydroxide. The hydroxides after being washed, were dissolved in nitric acid, and the earths reprecipitated from the dilute nitrate solution by dilute ammonia, washed free from alkali, and dissolved in formic acid.

Five large fractions of formates were obtained by the slow evaporation of the formate solution, and the earths remaining in solution were precipitated by ammonia. The earths in the large first formate fraction were converted into nitrates, hydroxides, and formates successively, and fractionated partly as formates (three fractions) and as hydroxides (last four fractions). The earths in the other formate fractions were precipitated fractionally with dilute ammonia. The atomic weights determined were:

Series I

Formate Fractions	I	II	III	IV	V	VI
Subdivisions..................	143.5	137	134	132	138.1	119.9
	....	....	....	....	132.4	....
	....	....	....	....	131.1	....
	....					
	....					
	135.1					
	63.0					

The last fraction of the formate fraction I, showing an atomic weight of 63, gave a white oxide and its solution showed no absorption spectrum. It consisted of yttrium and scandium.

The fractions derived from the large formate fractions I and II were separated further by fractional precipitation of the stearates. Thirty-three fractions thus obtained were combined into six groups according to the color of the oxides and their relation to the other fractions, the more soluble of one group being combined with the less soluble portion of the group following. (Series II)

The six groups were fractionated further as stearates into twenty-eight fractions, the atomic weights being determined.

SERIES III

138	146.9	144.7	150.8	144.8	146.5
....	....	....	....	....	....
....	....	....	....	....	....
....	....	....	147.5	....	....
....	128.9	131.6		....	
....				124.6	
113.6					

In the first part of the work, the atomic weights of only the extreme fractions were determined. This course is not advisable since the first fraction of a group is usually lower in atomic weight than the second, and often approximates an average of the group. It is to be expected with the earths under consideration, that the didymiums would be present to a greater extent in the first fractions of a series and the atomic weight of some intermediate fraction would be greatest. The atomic weights in many of the tables confirm this statement. It is therefore necessary in accurate work to determine the atomic weights of practically all the fractions of a series.

The fractions last described were combined according to the atomic weights into eight groups, the atomic weights of which approximated 148, 145, 142, 140, 137, 132, 128, 124. The first three groups, after removal of the cerium by hydrogen peroxide and ammonia, were taken for further separation as stearates. The atomic weights of the different groups and fractions are given. Each group was obtained by combination of fractions of the preceding group which had nearly the same atomic weight.

SERIES IV

At. wt. of group	(148)	(145)	(142)
" " " fractions	145.8 .... 131.3	146 .... 121.6	148.4 .... 137.6

SERIES V

At. wt. of group	(146)	(144)	(140)
" " " fractions	146.2 147.5 147.4 .... 120.1 118.9	148 139.9	144 143.3 143.2 142.1 141.3 126

SERIES VI

At. wt. of group	(147.6)	(143)	(144)
" " " fractions	153.1 146.6 142.9	150.4 150.2 143.4	145.3 143.1 140.9 133.7

SERIES VII

At. wt. of group	(153.1)	(146.6)	(143.4)
" " " fractions	152.3 150.3 147.8	151.2 145.7	149.8 137.1

SERIES VIII

At. wt. of group	(150)	(147)
" " " fractions	149.1 151.3	149.8 142.8

SERIES IX

At. wt. of group,	(149.5)
" " " fractions	151.8 153.2 153.0 149.8

SERIES X

At. wt. of group	(153)
" " " fractions	153.3 153.0

The fractions had now become so small that it was considered advisable to combine them with fractions of the same atomic weight and absorption spectra, which had been obtained from the soluble double sulphate portion from monazite.

Series XI showed a constant atomic weight of 153. The oxide had a light chamois color. The absorption spectrum of a ten per cent solution of the nitrate was:

Europium.		Samarium.		Erbium.	
464	strong	471	faint	484.3	fairly strong
534.5	″	478		486.8	
592	faint	496.5	haze	543.6	fairly strong
		500		545	
		559	very faint	666	very faint.

The earth was europium with only the faintest traces of samarium and a small amount of erbium.

Fractions from Series VIII and IX having the atomic weight of 149.8 were found to be constant. The absorption spectrum of a 20 per cent nitrate solution was composed of strong lines of samarium, a few lines of erbium of medium strength, and one stronger one of praseodymium.

Samarium.		Erbium.		Praseodymium.	
463	faint	483–485	medium	595–604.5	strong
470–475	medium	542–544.8	medium		
497–501.5	strong	666.6	very faint		
531–535	medium.				

The earth was therefore samarium in a high degree of purity, being especially free from other members of the gadolinium group.

SOLUBLE DOUBLE SULPHATE PORTION FROM MONAZITE

The earths remaining in solution after the removal of the insoluble double potassium sulphates as described on page 6, were precipitated as oxalates, converted into oxides and fractionated as chromates. The earths of the first insoluble chromate fraction thus obtained (at. wt. 134) were separated as chromates into four fractions having the atomic weights 141, 145, 131, 122 in order of precipitation. Cerium was present in the first fraction and was separated as ceric hydrate.

The first three fractions were fractionated as stearates, the atomic weights of the successive groups and fractions being:

SERIES A

At. wt. of group	(141)	(145)	(131)
" " " fractions	142.7 143.5 145.7 139.4	150.1 150.0 150.2 146.3 136.6	134.1 133.1 130.9

SERIES B

At. wt. of group	(143)	(146)	(150)
" " " fractions	149.6 144.4	150.8 150.2 147.9	153.2 156.0 147.8

SERIES C

At. wt. of group	(.....)	(.....)	(150.5)	(147.8)	(144.4)
" " " fractions	154. 152.8 151.5 142.5	152.2 151.9 148.9	154.0 150.4 151.8 147.7	154.7 149.9 146.0 134.5	151.0 146.1 134.6

SERIES D

At. wt. of group	(154)	(152.8)	(152.2)	(151.8)	(151.0)	(144.4)
" " " fractions	156.0 153.3	152.6 152.5	154.0 151.4	153.0 151.0	155.5 151.8	145.2 143.0

---

[1] Muthmann and Böhm, Berichte Vol. 36, p. 42: Vol. 33, p. 49.

Series D contained some of the purest fractions from the insoluble double sulphate portion as well as those from series C. The second group of the series had an atomic weight of 152.8 and yielded two fractions of atomic weight, 152.6 and 152.5. The limit of the efficiency of the stearate separation had therefore been reached for this particular earth in the quantity at hand,—about 3 grams. Spectroscopic examination revealed the presence of a very slight trace of erbium, with a larger amount of samarium, although the atomic weight was near that of pure europium, 152, and the spectrum lines of this element were strong. The lines of the absorption spectrum of a ten per cent nitrate solution were:

Europium.		Samarium.		Erbium.	
485	faint	471	strong	484.3	faint
529	faint	478		486.8	
534.4	medium	498	medium	543	faint
592.6	strong			548.5	
597				666	faint

Fractions having the atomic weight of 156 and 155.5 gave an absorption spectrum of erbium and samarium (extremely faint) with practically the same lines as above with varying intensity. The gadolinium was not as pure as the europium.

Europium had therefore been obtained which contained only the slightest traces of erbium, with a very small quantity of samarium, while by the same method another sample had been obtained which contained some erbium with only the slightest traces of samarium. There can be no doubt as to the efficiency of the stearate separation although it does not appear advisable to effect the complete removal of erbium and samarium from the two samples of europium until larger portions of the earth can be obtained.

The samples of europium were obtained from the original monazite material after 59 series of fractionation yielding 204 fractions as shown below:

Double magnesium nitrates,—1 series of 3 fractions.
Double potassium sulphates,—1 series of 3 fractions.

INSOLUBLE DOUBLE SULPHATE PORTION.			SOLUBLE DOUBLE SULPHATE PORTION.		
Separated as	Series.	Fractions.	Separated as	Series.	Fractions.
Formates........	7	21	Chromates.....	1	4
Stearates........	32	120	Stearates.......	17	53
	39	141		18	57

RARE EARTHS FROM GADOLINITE

Twenty-five pounds of gadolinite from Norway were powdered and decomposed by boiling with concentrated hydrochloric acid. Repeated boiling of the residue after decantation of the acid solution, removed nearly all of the rare earths.

The resulting acid solution was evaporated to a thick syrup which solidified on cooling. This was heated to dryness to dehydrate the silica, boiled with concentrated hydrochloric acid to decompose the basic salts formed by the heating, (largely basic ferric chloride), and extracted with water. After filtration and neutralization of the excess of the acid with ammonia, the solution was made acid with hydrochloric acid. It was found necessary in all cases of neutralization with alkalies, to work with dilute solutions of both earth and alkali, thus avoiding local precipitation and the formation of globules which enclose some of the solution and which dissolve with difficulty even when the solution is made decidedly acid. A saturated solution of oxalic acid, together with some of the crystals of acid, was added as long as precipitation resulted.

The solution was decanted, brought nearer to neutrality with ammonia and more oxalic acid added. The addition of ammonia and oxalic acid was repeated as long as was necessary for complete precipitation. After the oxalic acid had been added in excess, ammonia alone was required to bring down more of the oxalates. The first oxalates were white, but near the end of the process the precipitate was yellow or red due to iron and cerium.

The oxalates were completely washed, dried, and ignited. The mixed oxides and carbonates were dissolved by being sprinkled carefully into hot concentrated nitric acid. The material did not dissolve at first, but turned dark brown with the evolution of carbon dioxide, until a certain condition of either temperature or concentration was reached, when vigorous action ensued and solution was effected. Hydrochloric acid fumes as well as those of nitric acid were evolved. R. J. Meyer[4] accounts for the retention of the hydrochloric acid by the formation of oxalo-chlorides, when the oxalates are precipitated from a solution of certain acidity. A heavy dark red liquid was formed from which red crystals separated on cooling. The acid solution thus prepared was diluted to a large volume and the excess of acid nearly neutralized with caustic soda. The excess of acid cannot be removed by heating on account of the formation of basic salts. The solution at this point was yellow.

DOUBLE SULPHATE FRACTIONATION

Sixteen liters of the nitrate solution (sp. gr. 1.1554 at 17°) had been obtained in the manner described. To this solution, 200 cc of a saturated solution of sodium sulphate were added, with vigorous stirring. Precipitation resulted at once. The solution was filtered after standing twelve hours. After concentration of the solution by evaporation and cooling, two more fractions were removed by the addition of sodium sulphate solution.

300 cc of saturated potassium sulphate solution were added to the filtrate from the double sodium sulphate precipitation, and the solution evaporated until a precipitate began to form. The precipitate was pink. 200 cc of sulphate solution gave a second fraction; the fifth and sixth fractions were each precipitated by 500 cc of the sulphate solution, and each of the following fractions was precipitated by the addition of one liter of the sulphate solution until 18 fractions had been obtained and precipitation was complete. The didymiums were nearly removed in fraction 12, as shown by the color of the oxide and by the absorption spectrum of the nitrate solution. Fractions 16, 17 and 18 gave white oxides.

---

[4] (Abegg Handbuch III, Part I, page 148).

FORMATE FRACTIONATION

The double sulphate fractions were converted into hydroxides by boiling with concentrated sodium hydroxide solution. The hydroxides were only partially soluble in formic acid, and were therefore dissolved in nitric acid after washing to remove the greater part of the alkali, reprecipitated by dilute ammonia, and washed free from alkali, since the crystallization of the formates is influenced by the presence of alkali salts. The hydrates were dissolved in the minimum amount of formic acid (sp. gr. 1.23). The formate solution was slowly evaporated until considerable deposition had occurred. The solution was filtered and evaporated again, and the process repeated until the solution became syrupy and no more crystals could be obtained. The earths remaining in solution were precipitated by ammonia. Slow evaporation was found to be essential to the success of the process. The formates were decomposed by nitric acid and the earths precipitated as oxalates and ignited, in preference to drying and igniting the formates directly.

The eighteen double sulphate fractions had been divided into fifty-nine fractions by the crystallization of the formates. The color of the oxides, which varied from a red-brown to white, and the absorption spectrum of a 10 per cent solution of the nitrates served as a basis for the combination of these fractions into eight groups, the atomic weights of which were found later to be,—138.6, 121.1, 108, 105, 100, 102, 98.6, 99.9.

The four fractions of higher atomic weights were fractionated as double potassium sulphates, the atomic weights being:

At. wt. of group	(138.6)	(121)	(108)	(105)
At. wt. of fractions	135	136	120.2	118.3
	....	....	107.8	107.4
	133	....	105	101

These fractions were combined according to atomic weight and the three heavier groups, after removal of cerium, were fractionated as stearates. The atomic weights were:

At. wt. of group	(136)	(135)	(133)
At. wt. of fractions	138.2	136.1	140.9
	135	135.6	134.5
	127.2	124.8	....

The heavier fractions contained only a small amount of the gadolinium earths desired in our work,—erbium, samarium, showing faint lines in the spectrum. Lanthanum and the didymiums constituted the major portion of these fractions. The gadolinite was richest in yttrium and contained but little of the earths of higher atomic weight. Work with these earths was therefore abandoned, and the gadolinium earths extracted and separated from monazite as described.

The material from gadolinite had been subjected to 27 series of separations yielding 109 fractions,

Double sodium sulphate separation	1	series	of	4	fractions
" potassium sulphate "	1	"	"	18	"
Formate separation	18	"	"	59	"
Double potassium sulphate separation	4	"	"	12	"
Stearate separation	3	"	"	6	"
	27	"	"	109	"

THE STEARATE SEPARATION OF THE CERIUM EARTHS

The efficiency of the stearate separation when applied to the earths of the cerium group is shown by series V (page 8) where groups of the atomic weights 140, 144, and 146 were fractionated, also by series VI, and certain groups in series VII, and IX, in the insoluble sulphate portion. Series A, B, C, D (page 10) in the soluble sulphate portion show the same efficiency.

Spectroscopic examination of the groups and fractions indicated a partial separation of the didymiums, while cerium was concentrated in the first few fractions as shown by the hydrogen peroxide and ammonia test.

While none of the members of this group were isolated, the separations effected in this group while seeking the members of the gadolium group leave no doubt as to the efficiency of the stearate separation in the cerium group.

ATOMIC WEIGHT DETERMINATION[5]

For the determination of the atomic weights, about one gram of the oxide was weighed out roughly, sprinkled into 3 or 4 cc of concentrated nitric acid and heated. The solution thus effected was evaporated to a thick syrup which dissolved in water. When working with fractions rich in cerium earths, a basic salt separated out on dilution and heating, in which cases it was necessary to use more acid and to avoid heating as much as possible.

The acid solution was diluted to 800 cc and heated to boiling, and a cold saturated solution of pure oxalic acid added drop by drop. The solution was thoroughly stirred during precipitation, allowed to stand a minute, when the supernatent liquid was tested with a few drops of oxalic acid solution. The oxalate settled rapidly if the solution had been heated sufficiently before precipitation. The solution was allowed to stand over night, when the liquid was decanted on to a filter and the oxalate washed five times with boiling water by decantation, thrown onto the paper and there washed five times. The oxalate was dried at 110°–120°.

The dry oxalate was thoroughly pulverized in an agate mortar, and two portions of about 0.2 grams weighed out, one for the determination of the oxide ratio and the other for the acid ratio. One portion was ignited in a platinum crucible to constant weight. The percentage of R_2O_3 was thus determined. The other portion was suspended in 100 cc of water, and solution effected by addition of 8 cc of concentrated sulphuric acid. The solution was diluted to 400 cc, heated to about 80° and the oxalic acid liberated was titrated with a standard potassium permanganate solution. The percentage of C_2O_3 was thus determined. From the two determinations, the atomic weight of the earth was calculated.

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[5] Urbain. Bul. Soc. Chim. de France 1909 page 133.
R. J. Meyer (Abegg Handbuch Vol. III. 1 page 172).
Baxter and Daudt. Journ. Amer. Chem. Soc. Vol. XXX, page 563.

SUMMARY OF EXPERIMENTAL WORK

After division by potassium double sulphate, the rare earths from monazite were fractionated as stearates, until the gadolinium earths were concentrated and separated. Eighteen series of 57 fractions from the soluble double sulphate portion yielded a fraction of constant atomic weight of 152.5, which was practically pure europium. A second sample of europium (atomic weight 153), containing a trace of erbium, was separated from the insoluble double sulphate portion by 39 series of 141 fractions. The separation at the same time yielded a sample of impure gadolinium of atomic weight of 156, which contained some erbium, samarium, and europium, and also a sample of samarium of atomic weight 149.8.

The rare earths were extracted from twenty-five pounds of gadolinite and fractionated by 31 series of 129 fractions. The mineral contained quantities of the gadolinium earths too small to warrant their separation.

In the entire work 90 series of fractionations yielded 333 fractions of which 159 were analyzed and the atomic weight of the earth determined.

CONCLUSIONS

The experimental work described demonstrates that:

1. The gadolinium earths may be concentrated and separated by their fractional precipitation as stearates.

2. The stearate method is also applicable to the separation of the members of the cerium group.

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ON THE ADDITION OF ORGANIC ACIDS TO UNSATURATED HYDROCARBONS

BY
ARTHUR F. SIEVERS

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ON THE ADDITION OF ORGANIC ACIDS TO UNSATURATED HYDROCARBONS

INTRODUCTION

With the exception of the polymerization of acetylene and its homologues, no systematic study appears to have been made of the additive capacity of unsaturated hydrocarbons in so far as other carbon compounds are involved.

Inasmuch as a number of observations and experiments, that have been made in this laboratory from time to time, have led up to the present systematic study of this subject, the more significant ones may here be recorded:

In 1894 Mayer[1] made some observations on the angle of rotation of limonene in various optically inactive solvents. He drew the following conclusions from his results: "It is apparent that the solvents employed, viz.: absolute and ordinary alcohol, chloroform and glacial acetic acid, diminish the rotary power of limonene. In the case of absolute alcohol and chloroform the rotatory power of the limonene seems to decrease with fair regularity as the quantity of solvent increases. In the case of glacial acetic acid no such regularity is apparent."

These observations were pursued somewhat farther by Schreiner and Neumann.[2] Inasmuch as the results obtained have never been published, some of them may here be recorded. The experiments were begun by Neumann during the academic year 1900–1901, redeterminations being made by Schreiner in 1902. While the seal of most of the bottles in which these solutions were kept had been injured, some of them were still perfect.

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[1] *Am. Chem. Journ.*, 17, p. 692.

[2] E. C. Neumann: *Thesis submitted for the degree of Graduate in Pharmacy, U. W.*, 1901.

It was possible therefore to supplement the observations of Neumann extending over but a few months by observing the angle of rotation after a lapse of five years. This was done, and the following data were obtained, which, for the sake of comparison, are placed side by side with those obtained by Neumann and Schreiner.

Solution	1901	1902	1907
Pure Limonene	104.80	102.00	104.60
Limonene + acetone	36.50	35.00	35.10
Limonene + chloroform	37.14	35.90	35.90
Limonene + ether	36.80	34.30	33.66
Limonene + alcohol	32.30	32.60	28.20
Limonene + glacial acetic acid	34.90	35.40	36.40
Turpentine oil + absolute alcohol	6.71	6.80	6.00

In 1897, at a time when the method of assaying alcoholic components of volatile oils by the acetylization method had come into general use, Professor Kremers became interested in the problem of the influence of the unsaturated hydrocarbons present on the result of the assay. Even if it were not regarded probable that the acetic acid anhydride used in the assay should add to the hydrocarbon, acetic acid might, as had indeed been shown.[3] Inasmuch as most volatile oils contain some moisture the conversion of at least a small part of the acetic acid anhydride to anhydrous acetic acid could be explained. In oils rich in alcohol such a change might become the cause of an insignificant error, but how in oils with but a low alcohol content?

With such a priori conceptions, the results obtained by actual tests were astounding. Preliminary experiments were made with limonene, pinene and caryophyllene. A mixture of 10 cc of the hydrocarbon, 10 cc of acetic acid anhydride and 2 gms. of anhydrous sodium acetate were heated for one hour and then treated according to the usual acetylization method. The results obtained by Martha M. James at that time are herewith recorded:

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[3] Bouchardat et Lafont, *Compt. rend.*, 102, p. 171.

Description of hydrocarbon	Amount of ester calculated as $C_{10}H_{17}O.COCH_3$	
	I	II
Limonene from oil of Sweet Orange. Fraction 174°-176°	29.35	29.1
Turpentine—commercial, crude	4.0	3.8
Turpentine, rectified	3.9	3.6
Turpentine—rectified and dried with calcium chloride	2.4	2.7
Turpentine—rectified, dried with calcium chloride and fractionated (150°-156°)	3.3	

These results were so striking that they were stated to Dr. C. Kleber and Dr. Best during the summer of 1896 while Professor Kremers was in the factory of Fritzsche Bros. at Garfield, for the purpose of studying some of the practical problems that presented themselves in the revision of the U. S. P. tests on volatile oils. These gentlemen were naturally skeptical, but their curiosity was sufficiently roused to test the matter. Having on hand a carefully fractionated pinene prepared some months previously and kept in a cool dark cellar, Dr. Best obtained results much higher than those obtained by Miss James for the same hydrocarbon.

Not satisfied, Professor Kremers requested Mr. J. A. Anderson to repeat some of the experiments previously made by Miss James. His results are herewith recorded:

DESCRIPTION OF HYDROCARBON	AMOUNT OF ESTER CALCULATED AS $C_{10}H_{17}O.COCH_3$	
	I	II
Limonene — fraction 174°-178°	50.16	49.5
Limonene — fraction 176°-178°	62.7	66.2
Turpentine oil — crude	7.51	7.33

Before proceeding to record the results of more systematic experimentation, it will be necessary briefly to review the work that has thus far been recorded on this subject. The results found may be briefly summarzied by tabulating the unsaturated hydrocarbons and the organic compounds that have been added to each of these.

PINENE

- I. Alcohols
  - 1) Trinitrophenol
- II. Aldehydes
  - 1) Formaldehyde
- III. Acids
  - 1) Acetic acid
  - 2) Benzoic acid
  - 3) Oxalic acid

LIMONENE AND DIPENTENE

- I. Alcohols
- II. Aldehydes
  - 1) Formaldehyde
- III. Acids

CAMPHENE

- I. Alcohols
- II. Aldehydes
- III. Acids
  - 1) Formic acid
  - 2) Acetic acid

FENCHENE

- I. Alcohols
  - 1) Ethyl alcohol
- II. Aldehydes
- III. Acids
  - 1) Acetic acid

If, finally, it be borne in mind that some of the processes patented for the semi-artificial preparation of camphor involve the addition of organic acids to the pinene of turpentine oil, it must become apparent that there exist abundant reasons, both purely theoretical as well as practical, which seem to demand a careful and systematic study of the entire problem of the addition of organic compounds, more particularly of organic acids, to unsaturated hydrocarbons. A beginning has been made and the results thus far obtained not only justify the time spent on this problem, but invite a much more extensive investigation of the entire field.

THE ADDITION OF GLACIAL ACETIC ACID TO DEXTRO PINENE

The pinene used in the following experiments was obtained from commercial American oil of turpentine. The oil was first rectified by shaking with an aqueous solution of caustic potash and subsequent distillation. The first three-fourths of the oil thus rectified were then fractionated into five fractions and the specific gravity and angle of rotation of the three pinene fractions taken. The results of the fractionation are herewith tabulated.

Fraction	$(D)_{20°}$	$(\alpha)_{20°}$
1. —155°		
2. 155°—156°	0.8560	+15° 50′
3. 156°—157°	0.8564	+14° 14′
4. 157°—160°	0.8585	+11° 41′
5. 160°+		

For the following experiments fractions 2 and 3 were used. They were mixed and their physical constants retaken. These were found to be as follows: Sp. gr. at 20° C. 0.8575; angle of rotation at 20° C + 15° 0′.

500 cc. of this pinene mixture were mixed with an equal volume of glacial acetic acid. At the same time another 500 cc. of the pinene were mixed with two volumes of glacial acetic acid. The physical constants of both mixtures were immediately taken. After that the constants were taken every ten days for some time, but the changes were so small that they were finally taken only once a month.

TABLE I

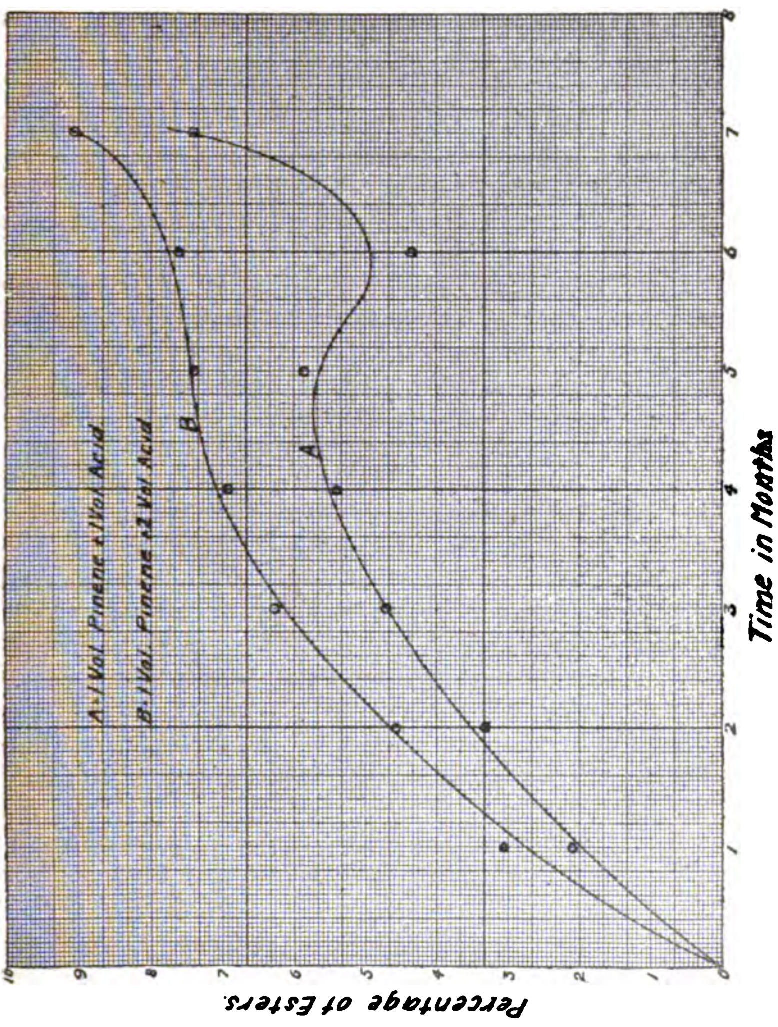
1 Volume of Pinene + 1 Volume of Acid

Date	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Aug. 27	0.9400	+8° 41′	....	....	....
Sept. 21	0.9400	+8° 35′	....	....	....
Oct. 5	0.9430	+8° 14′	....	....	....
Oct. 12	0.9428	+8° 15′	....	....	....
Oct. 22	0.9457	+7° 35′	....	....	....
Nov. 1	0.9450	+7° 50′	3.92	1.36	2.09
Nov. 11	0.9454	+7° 40′.	....	....	....
Nov. 21	0.9463	+7° 54′	....	....	....
Dec. 3	0.9464	+7° 32′	....	....	....
Dec. 13	0.9460	+7° 45′	6.26	2.18	3.32
1907					
Jan. 3	0.9477	+7° 30′	....	....	....
Jan. 13	0.9477	+7° 20′	8.75	3.06	4.69
Feb. 13	0.9480	+7° 10′	9.97	3.49	5.46
Mar. 15	0.9497	+7° 12′	10.85	3.79	5.82
Apr. 16	0.9500	+7° 20′	8.15	2.86	4.36
May 15	0.9502	+7° 18′	13.80	4.84	7.40

TABLE II

1 Volume of Pinene + 2 Volumes of Acid

Date	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Aug. 27	0.9744	+6° 8′	....	....	....
Sept. 21	0.9744	+6° 6′	....	....	....
Oct. 5	0.9757	+5° 38′	....	....	....
Oct. 12	0.9757	+5° 15′	....	....	....
Oct. 22	0.9767	+4° 50′	....	....	....
Nov. 1	0.9769	+4° 50′	3.62	1.27	3.03
Nov. 11	0.9770	+4° 47′	....	....	....
Nov. 21	0.9789	+4° 45′	....	....	....
Dec. 3	0.9783	+4° 46′	....	....	....
Dec. 13	0.9785	+4° 35′	5.80	2.03	4.83
1907					
Jan. 3	0.9797	+4° 28′	....	....	....
Jan. 13	0.9788	+4° 30′	7.46	2.61	6.27
Feb. 13	0.9795	+4° 20′	7.94	2.78	6.58
Mar. 13	0.9814	+4° 17′	8.87	3.10	7.41
April 16	0.9806	+4° 18′	9.15	3.20	7.60
May 15	0.9804	+4° 15′	10.87	3.80	9.05


A-1 Vol. Pinene + 1 Vol. Acid
B-1 Vol. Pinene + 2 Vol. Acid
A
B
Percentage of Esters
Time in Months
0
1
2
3
4
5
6
7
8
9
10

THE ADDITION OF GLACIAL ACETIC ACID TO DEXTRO LIMONENE

Preparation of Material

The limonene used in the following work was received through the liberality of Dr. S. H. Baer, at that time with Mergentine & Lamm of New York, who had obtained it as by-product in the preparation of a concentrated oil of orange from a crude oil of orange.

The specific gravity in 1906 was 0.8530 at 20° C.; the angle of rotation + 87° 45′ at 20° C.; saponification number 11.84, and acetylization number 26.6.

A small portion of the material was reserved. The bulk of the crude limonene was subjected to a thorough purification. It was first shaken several times with several portions of sodium acid sulphite solution to remove any aldehydes. However the odor of the limonene underwent no perceptible change due to this treatment. In order to determine whether any traces of aldehyde had been removed, the sulphite solution was neutralized with an excess of sodium carbonate and distilled. The distillate had a very decided odor of citronellal. In order to get a positive test for aldehyde the distillate and also the residue were shaken out with ether separately and the ethereal solutions mixed. These upon evaporation left a small quantity of a heavy, syrupy, brown liquid which gave a positive test for aldehyde with magenta solution.

After the removal of the aldehydes the sp. gr. was found to be 0.8562 at 20° C.; the angle of rotation + 92° 47′ at 20° C.; and the saponification number 6.9 and 6.23 respectively.

Since the saponification number of the limonene indicated an appreciable quantity of esters, it was deemed best to saponify the entire quantity. The necessary quantity of caustic potash calculated from the saponification number was dissolved in alcohol and mixed with the limonene. The mixture was then boiled on a water bath for two hours. After cooling the limonene was distilled over with steam. A perfectly clear, colorless product was obtained whereas the crude product had been decidedly yellow.

The constants of the limonene thus rectified were found to be: sp. gr. 0.8440 at 20° C.; angle of rotation +96° 37′ at 20° C.; acetylization number 10.1.

The rectified limonene was fractionated into four fractions. The specific gravity and the angle of rotation were taken of each fraction. The following tabulation gives a summary of the fractionation, the constants, and the volume of each fraction.

Fraction	Volume in cc	$(D)_{20°}$	$(\alpha)_{20°}$
— 175°	88	0.8413	+93° 49′
175° — 176.5°	1108	0.8434	+98° 15′
176° — 180°	476	0.8455	+98° 51′
180°+	74	0.8723	+81° 0′

For the sake of better comparisons the data obtained in the several experiments described above are herewith tabulated again:

Description of limonene	$(D)_{20°}$	$(\alpha)_{20°}$	Sap. No.	Ester No.
Crude	0.8530	+87° 45′	11.45	26.6
Shaken out with $NaHSO_3$	0.8562	+92° 47′	6.56	....
Saponified	0.8440	+96° 37′	4.0*	10.1
Fraction — 175°	0.8413	+93° 49′	3.16*	....
Fraction 175°—176.5°	0.8434	+98° 15′	2.65*	7.6
Fraction 176.5°—180°	0.8455	+98° 51′	1.30*	14.4
Fraction 180°+	0.8723	+81° 0′	5.06*	51.00

* Determinations made five weeks after rectification and fractionation.

FORMATION OF THE ESTERS

In the experiments which follow the limonene from fraction 175°-176.5° was used. The object was to ascertain the rate of ester formation of the limonene with the glacial acetic acid, and the extent to which this formation is indicated by the specific gravity and the angle of rotation of the mixture.

Two different mixtures of the limonene and the glacial acetic acid were made. The first mixture consisted of one volume of limonene and one volume of glacial acetic acid. The second mixture consisted of one volume of limonene and two volumes of the acid.

To determine the effect of so-called catalytic agents on the rate of ester formation in these mixtures, four more mixtures were made, two containing hydrogen chloride and two anhydrous sodium acetate.

The two mixtures containing sodium acetate were prepared as the previous ones, namely: one containing equal volumes of limonene and glacial acetic acid and the other containing one volume of limonene to two of the acid. To each of these mixtures were then added exactly 2.5 gms. of anhydrous sodium acetate and the mixtures agitated frequently until the acetate was dissolved.

Two more mixtures were prepared to each of which were added the molecular equivalent of 2.5 gms. of anhydrous sodium acetate or 1.11 gms. of hydrogen chloride. In all these mixtures great care was taken to prevent any admixtures of traces of moisture. It was, therefore, necessary to add the hydrogen chloride in some anhydrous form and not in the form of the ordinary aqueous test solution. The method adopted was as follows: Hydrogen chloride was generated from common salt with sulphuric acid and passed first through a wash bottle containing sulphuric acid, and then through a bottle with calcium chloride. The gas, which after this treatment was regarded as dry, was then passed into glacial acetic acid. The percentage of hydrogen chloride in the acid was then determined gravimetrically with silver nitrate as insoluble silver chloride.

A quantity of this acid containing exactly 1.11 gms. of hydrogen chloride was weighed off, diluted to the desired volume and mixed with the limonene as in the previous mixtures.

The specific gravity and angle of rotation of these mixtures were taken immediately after they had been mixed and after that, with as much regularity as possible, at intervals of ten days. The changes found in the constants in ten days were so small, however, that they were finally taken only once a month. Once during each month of observation the amount of ester formed was determined by means of the acetylization number.

In determining the acetylization number considerable difficulty was met with at first due to the strong acetic acid solution. After considerable experimentation the following method was found to give very accurate results: About 8 gms. of the mixture are weighed carefully and then transferred to a 250 cc. flask and a few drops of phenolphthalein added. An alcoholic potassium hydroxide solution containing about 50 gms. of potassium hydroxide to the liter is then added slowly to neutralize the acetic acid. The flask must be kept carefully cooled during the addition of the alkali in order to prevent the decomposition of any esters due to a rise in temperature. When exactly neutral, 10 cc. of a standard alcoholic potassium hydroxide solution are added and the mixture boiled for half an hour on a water bath. After cooling the excess of alkali is titrated back with ½ N. Sulphuric Acid V. S.

TABLE I

1 VOLUME OF LIMONENE + 1 VOLUME OF ACID

Date	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	p. c. of ester	p. c. as ester
Nov. 29, 1906........	0.9380	+47° 30′	....	....	....
Dec. 8, 1906........	0.9384	+47° 45′	....	....	....
Dec. 18, 1906........	0.9390	+47° 33′	....	....	....
Jan. 4, 1907........	0.9388	+47° 10′	1.84	0.64	1.00
Feb. 12, 1907........	0.9390	+47° 45′	3.35	1.17	1.80
Mar. 15, 1907,........	0.9392	+47° 32′	3.37	1.18	1.82
Apr. 15, 1907........	0.9398	+47° 30′	3.86	1.35	2.09
May 15, 1907........	0.9400	+47° 0′	3.81	1.33	2.06

TABLE II

1 VOLUME OF LIMONENE + 2 VOLUMES OF ACID

Date	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	p. c. of ester	p. c. as ester
Nov. 29, 1906........	0.9733	+31° 52′	....	....	....
Dec. 8, 1906........	0.9733	+31° 45′	....	....	....
Dec. 18, 1906........	0.9730	+31° 25′	....	....	....
Jan. 4, 1907........	0.9737	+31° 0′	1.07	0.37	0.89
Feb. 12, 1907........	0.9828	+31° 15′	2.03	0.71	1.70
Mar. 15, 1907........	0.9744	+31° 25′	3.35	1.17	2.84
Apr. 15, 1907........	0.9755	+31° 35′	3.35	1.17	2.84
May 15, 1907........	0.9748	+31° 43′	3.26	1.14	2.74

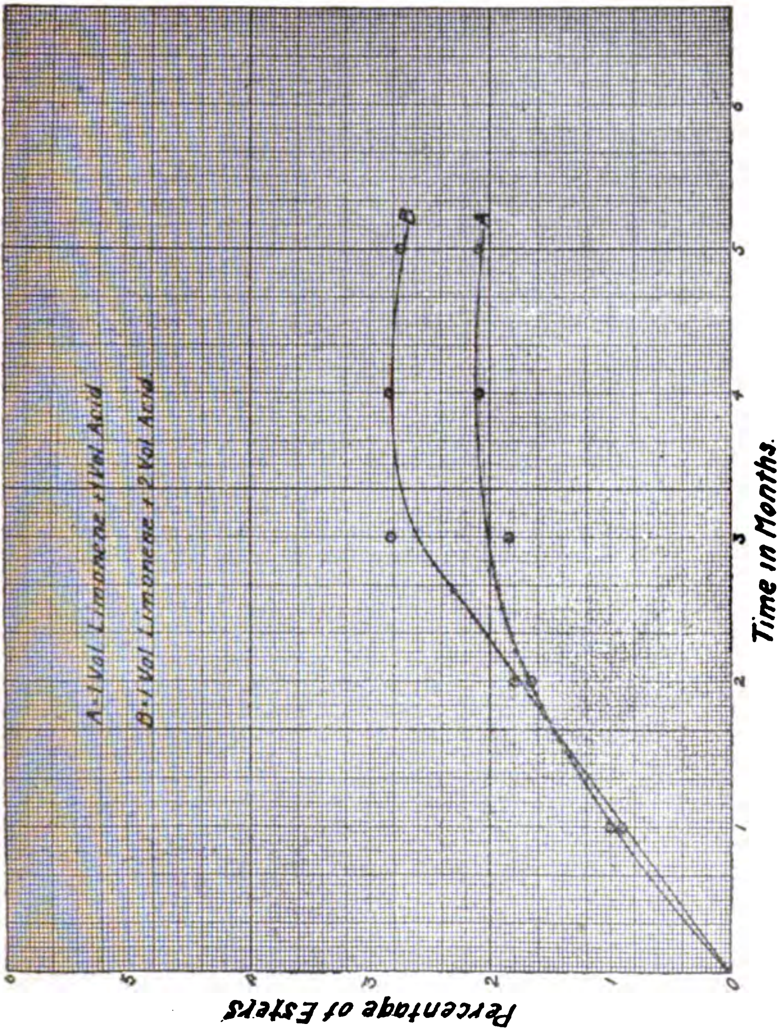

A-1 Vol. Limonene +1 Vol. Acid
B-1 Vol. Limonene +2 Vol. Acid
A
B
Percentage of Esters
0
1
2
3
4
5
6
Time in Months.
0
1
2
3
4
5
6

TABLE III

1 VOLUME OF LIMONENE + 1 VOLUME OF ACID + 1.11 GMS. OF HCl

Date	$(D)_{20°}$	$(\alpha)_{20°}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Nov. 29	0.9390	+47° 35′	....	....	....
Dec. 8	0.9389	+48° 00′	....	....	....
Dec. 18	0.9390	+47° 40′	....	....	....
1907					
Jan. 4	0.9403	+47° 20′	3.00	1.08	1.68
Feb. 12	0.9430	+46° 40′	3.50	1.22	1.92
Mar. 15	0.9402	+47° 38′	5.41	1.89	2.93
Apr. 15	0.9441	+47° 34′	4.20	1.47	2.28
May 15	0.9408	+46° 45′	5.09	1.78	2.78

TABLE IV

1 VOLUME OF LIMONENE + 2 VOLUMES OF ACID + 1.11 GMS. OF HCl

Date	$(D)_{20°}$	$(\alpha)_{20°}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Nov. 29	0.9742	+31° 50′	....	....	....
Dec. 8	0.9740	+31° 37′	....	....	....
Dec. 18	0.9740	+31° 20′	....	....	....
1907					
Jan. 4	0.9750	+31° 30′	2.65	0.92	2.23
Feb. 12	0.9746	+31° 15′	3.61	1.26	3.04
Mar. 15	0.9750	+31° 20′	3.73	1.30	3.14
Apr. 15	0.9764	+31° 35′	3.92	1.37	3.30
May 15	0.9754	+31° 25′	4.49	1.57	3.78

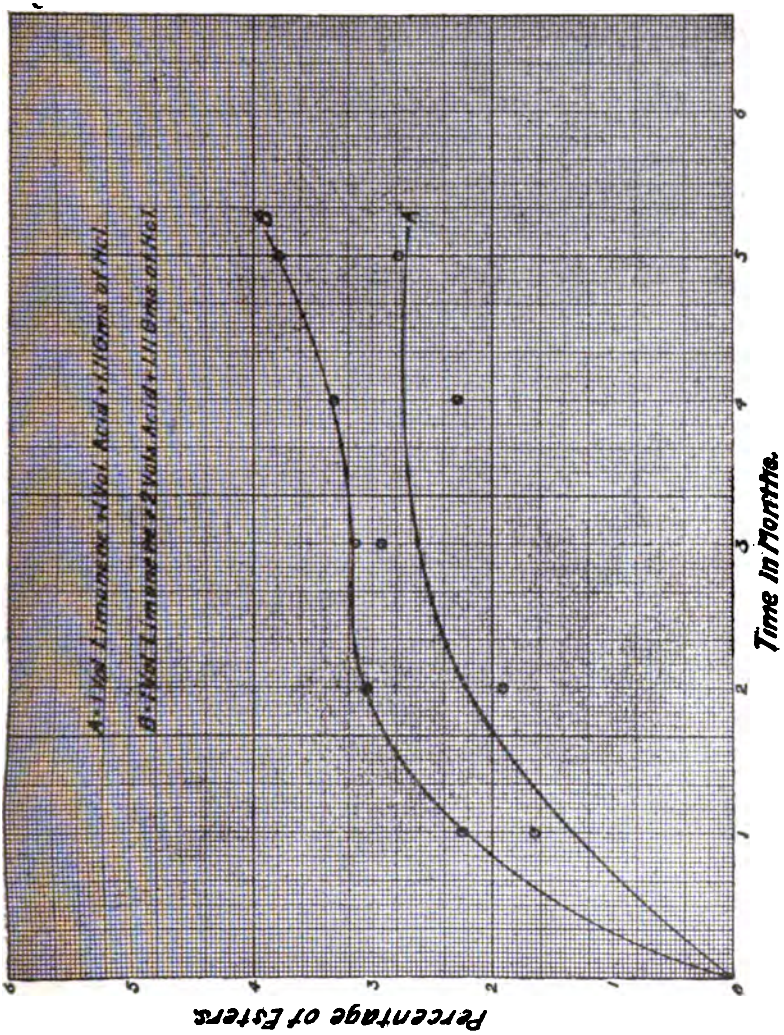

A-1 Vol. Limonene + 1 Vol. Acid + 1.1 Gms. of HCl.
B-1 Vol. Limonene + 2 Vols. Acid + 1.1 Gms. of HCl.
A
B
0
1
2
3
4
5
6
0
1
2
3
4
5
6
Time in Months.
Percentage of Esters

TABLE V

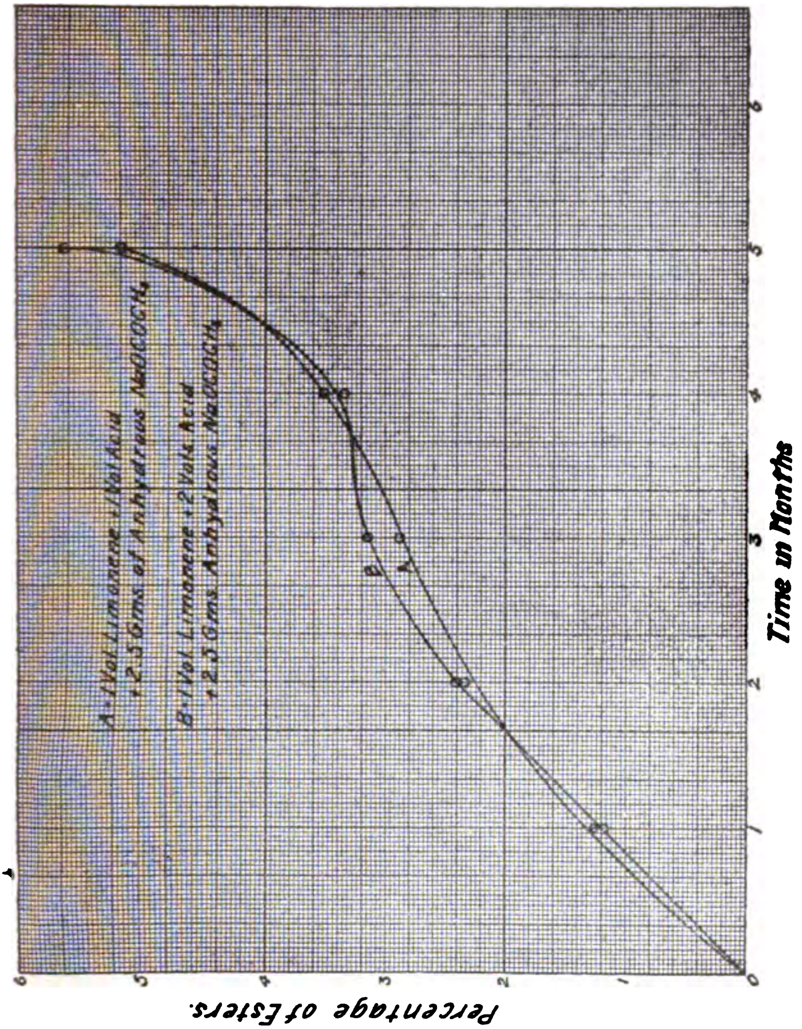
1 VOL. OF LIMONENE+1 VOL. OF ACID+2.5 GMS. OF ANHYD. Na $OCOCH_3$

Date	$(D)_{20°}$	$(\alpha)_{20°}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Nov. 29	0.9414	+47° 40′	....	....	....
Dec. 8	0.9416	+47° 37′	....	....	....
Dec. 18	0.9430	+46° 45′	....	....	....
1907					
Jan. 4	0.9440	+46° 25′	2.21	0.77	1.26
Feb. 12	0.9453	+46° 15′	4.32	1.51	2.35
Mar. 15	0.9464	+46° 0′	5.32	1.86	2.88
Apr. 15	0.9482	+45° 50′	6.49	2.27	3.55
May 15	0.9490	+45° 15′	9.47	3.32	5.19

TABLE VI

1 VOL. OF LIMONENE+2 VOLS. OF ACID+2.5 GMS. OF ANHYD. Na $OCOCH_3$

Date	$(D)_{20°}$	$(\alpha)_{20°}$	Ester No.	p. c. of ester	p. c. as ester
1906					
Nov. 29	0.9758	+31° 50′	....	....	....
Dec. 8	0.9764	+31° 40′	....	....	....
Dec. 18	0.9767	+31° 30′	....	....	....
1907					
Jan. 4	0.9758	+31° 4′	1.40	0.49	1.18
Feb. 12	0.9770	+31° 20′	2.85	0.99	2.40
Mar. 15	0.9785	+31° 0′	3.73	1.30	3.15
Apr. 15	0.9800	+31° 5′	3.94	1.38	3.33
May 15	0.9798	+31° 12′	6.75	2.36	5.70


A: 1 Vol. Limonene + 1 Vol. Acid
+ 2.5 Gms. of Anhydrous NaOCOCH$_3$
B: 1 Vol. Limonene + 2 Vols. Acid
+ 2.5 Gms. Anhydrous NaOCOCH$_3$
A
B
0
1
2
3
4
5
6
Time in Months
0
1
2
3
4
5
6
Percentage of Esters.

FORMATION OF ESTERS AT HIGHER TEMPERATURES AND UNDER INCREASED PRESSURE

In order to determine the effect of higher temperature and increased pressure the following experiments were conducted: Two mixtures of pinene and glacial acetic acid, one containing equal volumes of both, and the other one volume of pinene and two volumes of the acid, were placed in small pressure bottles and heated in a water bath. After heating for eight hours the physical constants and ester content were determined. Fresh mixtures were then heated under the same conditions for sixteen hours and the physical constants and ester content again determined. Finally similar mixtures were heated for twenty-four hours.

The temperature, 100° C., applied in this case was below the boiling point of the mixture, and as the amount of ester obtained was not very great, further experiments were performed with the same material in which higher temperatures were applied. In this case the bottles containing the mixtures were heated in an oil-bath at a temperature ranging from 140°-150° C. This temperature was chosen because it is above the boiling point of the glacial acetic acid and also above that of the mixture, whereas it is below that of the pinene. The time of heating was, as in the previous experiments, eight, sixteen, and twenty-four hours respectively.

The mixtures heated at the higher temperatures acquired a light straw color when heated for sixteen hours and a decided yellow color when heated for twenty-four hours.

The following tabulation shows the results obtained in the three different series of experiments.

TABLE I. 100° C

1 Volume of Pinene + 1 Volume of Acid

Time	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	D. C. of ester	D. C. as ester
8 hrs	0.9465	+4° 25′	10.18	3.77	5.80
16 hrs	0.9488	+3° 36′	13.80	4.83	7.42
24 hrs	0.9502	+3° 40′	15.54	5.44	8.37
1 Volume of Pinene + 2 Volumes of Acid					
8 hrs	0.9807	+2° 33′	10.30	3.60	8.58
16 hrs	0.9823	+2° 33′	14.43	5.05	12.10
24 hrs	0.9838	+2° 36′	15.70	5.49	13.12

TABLE II. 140° to 150° C

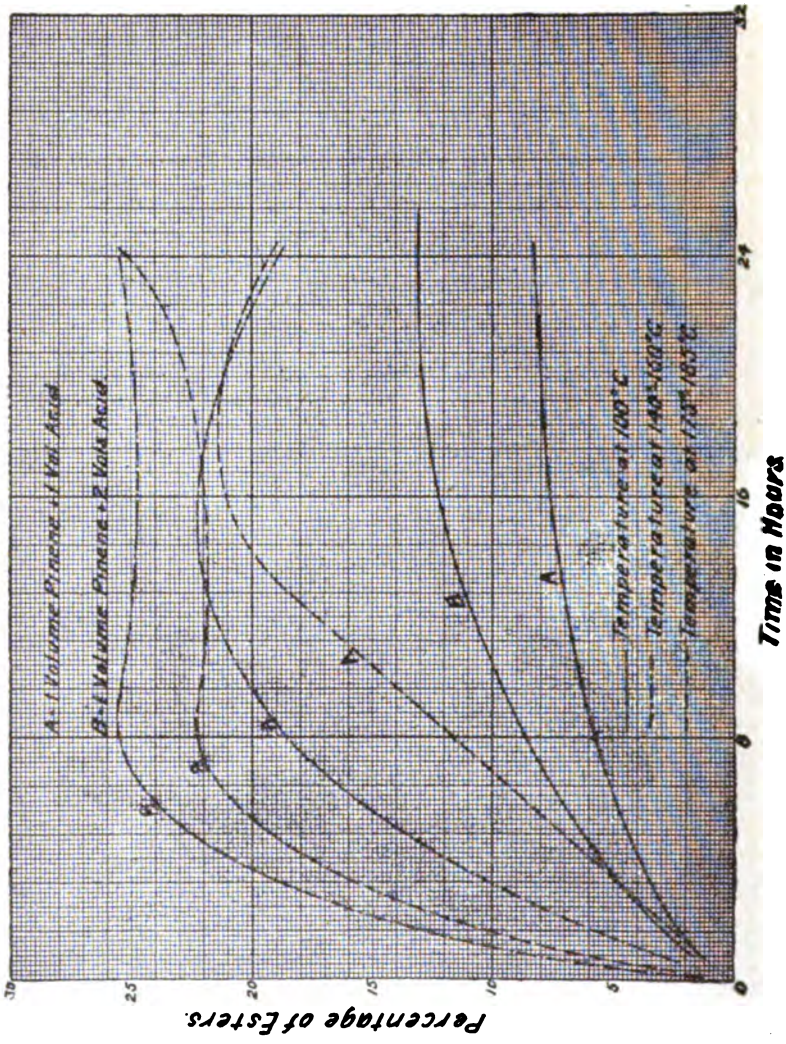
1 Volume of Pinene + 1 Volume of Acid

Time	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	D. C. of ester	D. C. as ester
8 hrs	0.9590	+4° 24′	34.50	12.09	18.78
16 hrs	0.9586	+4° 0′	40.90	14.30	22.26
24 hrs	0.9568	+3° 52′	34.92	12.21	18.90
1 Volume of Pinene + 2 Volumes of Acid					
8 hrs	0.9962	+2° 35′	30.10	10.52	25.50
16 hrs	0.9921	+2° 20′	29.45	10.30	24.80
24 hrs	0.9881	+1° 30′	30.20	10.58	25.40

TABLE III. 175° to 185° C

1 Volume of Pinene + 1 Volume of Acid

Time.	$(D)_{20^\circ}$	$(\alpha)_{20^\circ}$	Ester No.	D. C. of ester	D. C. as ester
8 hrs.......	0.9517	+3° 0′	21.12	7.39	11.5
16 hrs............	0.9509	+3° 25′	39.4	13.8	21.00
24 hrs............	0.9581	+3° 18′	35.10	12.13	19.1
1 Volume of Pinene + 2 Volumes of Acid					
8 hrs............	0.9895	+2° 37′	26.58	9.31	11.5
16 hrs............	0.9873	+3° 3′	26.1	9.14	21.97
24 hrs........ ...	0.9876	+1° 23′	30.10	10.52	25.3


A - 1 Volume Pinene + 1 Vol. Acid
B - 1 Volume Pinene + 2 Vols. Acid
Temperature at 100°C
Temperature at 140°-150°C
Temperature at 175°-185°C
A
B
A
B
A
B
0
5
10
15
20
25
30
Percentage of Esters.
0
8
16
24
32
Time in Hours

ESTER FORMATION UNDER ORDINARY PRESSURE

The preceding experiments show the extent of ester formation when the mixtures are heated in sealed tubes at various temperatures and for various intervals of time. In order to study the effect of the time of heating under normal pressure the following series of experiments were conducted. 300 cc. of a mixture of equal parts of pinene and glacial acetic acid were placed in a round bottomed flask of one liter capacity and connected with a reflux condenser. The mixture was heated slowly up to its boiling point when the heat was removed long enough to take a small sample from the flask. The heating was then continued for fifteen minutes when another sample was removed. In this way the experiment was continued, samples being taken out at definite intervals, such intervals being gradually increased as the heating continued. Towards the last the samples were taken out every two hours. Altogether the mixture was heated twenty hours. As the heating proceeded the material in the flask gradually darkened and at the close of the period had acquired a dark brown color.

The samples taken out in each case were just enough for one ester determination. No duplicate could therefore be made; neither could the specific gravity and angle of rotation be taken of each sample. The specific gravity and optical rotation of the mixture before heating were taken and found to be as follows, viz.: sp. gr. at 20°=0.9400; angle of rotation at 20°=+8° 40′.

After heating for twenty hours the specific gravity was found to be 0.9529 at 20° C. The optical rotation could not be taken on account of the dark color of the mixture.

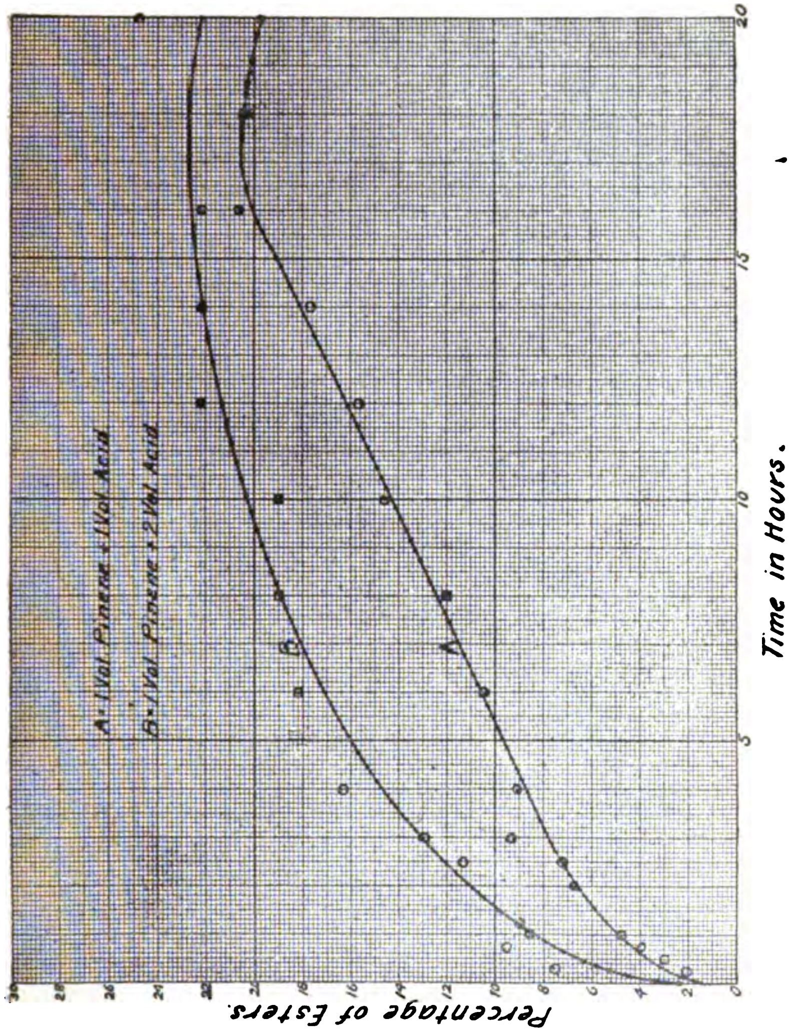
An exact duplicate of this experiment was made with a mixture of one volume of pinene and two volumes of glacial acetic acid. Samples were taken out at exactly the same intervals and the heating carried out under exactly the same conditions. In this case again the mixture gradually turned dark and after twenty hours of heating it also was of a dark reddish-brown color, slightly darker, however, than the preceding mixture.

The physical properties before heating were as follows: specific gravity at 20° C.= 0.9743; optical rotation at 20° C. =+6° 8′. After heating the specific gravity was 0.9888. Here again the optical rotation could not be taken on account of the dark color of the mixture.

The boiling point of the first mixture was 116.5° C. and that of the second was 116° C. In both cases the boiling point rose very gradually through about one degree during the process of heating.

The following is a tabulation of the ester number, percentage of ester, and percentage of pinene as ester in each sample. In order to calculate the true percentage of pinene as ester in the mixture it is necessary to know the specific gravity in each case. Since the specific gravity was not taken in each case the average of the specific gravities of the mixtures before and after heating was used in the calculations. It must therefore be borne in mind that the percentage as tabulated below is only a very close approximation. The average specific gravity of the first mixture was 0.9464 at 20°; that of the second was 0.9815 at 20°.

Time	1 Volume of Pinene + 1 Volume of Acid			1 Volume of Pinene + 2 Volumes of Acid		
	Ester No.	p. c. of ester	p. c. as ester	Ester No.	p. c. of ester	p. c. as ester
	2.56	0.89	1.37	2.90	1.01	2.39
15 min.	3.71	1.29	1.99	9.04	3.16	7.46
30 min.	5.51	1.93	2.96	......	......	......
45 min.	7.29	2.55	3.91	11.87	4.16	9.81
1 hr.	9.01	3.15	4.82	10.60	3.71	8.75
1:15	19.63	3.36	5.16	10.90	3.81	8.99
1:30	......	......	......	11.95	4.20	9.90
2 hrs.	12.53	4.38	6.71	......	......	......
2:30	13.30	4.65	7.13	13.50	4.73	11.15
3 hrs.	17.32	6.05	9.28	15.60	5.46	12.90
4 hrs.	16.80	5.89	9.02	19.70	6.90	16.30
6 hrs.	19.60	6.86	10.51	22.00	7.70	18.20
8 hrs.	22.60	7.91	12.10	23.05	8.05	19.00
10 hrs.	28.30	9.55	14.63	23.00	8.05	19.00
12 hrs.	29.30	10.24	15.70	26.80	9.36	22.18
14 hrs.	31.10	10.84	16.68	26.80	9.39	22.18
16 hrs.	38.60	13.32	20.70	26.78	9.37	22.10
18 hrs.	38.05	13.31	20.40	25.20	8.82	20.90
20 hrs.	36.60	12.81	19.61	30.00	10.50	24.80


A = 1 Vol. Pinene + 1 Vol. Acid
B = 1 Vol. Pinene + 2 Vol. Acid
A
B
Time in Hours.
Percentage of Esters.
0
5
10
15
20
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30

ADDITION OF PICRIC ACID TO PINENE

Bornyl picrate was prepared according to Tilden and Forster[4] in the following way: 20 gms. of chemically pure picric acid were mixed with 200 cc. of rectified turpentine oil in a round bottomed liter flask connected with a reflux condenser. No reaction was observed in the cold, and the acid, being insoluble in the turpentine oil, settled at the bottom. The temperature was slowly raised by means of a low flame. As the temperature rose the mixture gradually acquired a reddish color which changed to dark red-brown when 150° was reached. At this temperature the mixture began to crack and the evolution of heat was almost sufficient to keep the temperature at 150° without the aid of a flame. After heating for about one hour the mixture was allowed to cool somewhat, after which the liquid portion was poured into a beaker and set aside in a cool place to crystallize. The black tarry residue which remained in the flask was examined later.

After about twelve hours small clusters of crystals began to form on the sides of the beaker containing the liquid, and after twenty-four hours the crystallization was interrupted, the mother liquid set aside for further crystallization, and the crystals removed for purification. On the bottom of the beaker was a layer of tarry material resembling that which remained in the original flask.

The crystals were rubbed in a mortar with several portions of water to remove the picric acid. They were then transferred to a flask and boiled with alcohol until all were dissolved. Upon cooling the crystals again separated in the form of small yellow scales. After draining on a force filter and washing several times with small portions of alcohol, the crystals were allowed to dry and were then transferred to a bottle.

Upon standing in diffused daylight the crystals soon became darker in color, changing from a bright yellow to a yellowish-brown. That side of the bottle which was exposed to the direct light of the window changed color much more quickly.

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[4] *Journ. Am. Chem. Soc.*, 1893 I, p. 1388.

The mother liquid, after standing for several hours, showed no signs of further crystallization and was therefore taken and distilled with steam. A colorless oily layer separated from the aqueous distillate. This material which had a distinct pinene odor was separated and fractionated. It distilled at a temperature ranging from 150° to 159° C., the bulk of it distilling at 155° to 157°. The specific gravity of the main fraction was found to be 0.8599 at 20° C. and the angle of rotation was +5° 40′.

Judging from the odor, boiling point, and specific gravity, the material was pinene with a greatly reduced optical activity.

Saponification of the "Ester"

The bornyl picrate was mixed with a molecular quantity of potassium hydroxide in alcohol and boiled on a water bath for about one hour. The mixture turned to a dark brown color After cooling, the material was distilled with steam. The first distillate consisted mainly of alcohol with a strong camphoracous odor. Upon further distillation small crystals began to separate on the sides of the flask and condenser and also in the receiver. After no more crystals came over the distillation was stopped and the borneol collected and drained on a filter. It consisted of fine white crystals.

ACTION OF GLACIAL ACETIC ACID ON AMYLENE

In order to ascertain whether esters of the unsaturated hydrocarbons of the olefine series could be obtained in like manner, the action of glacial acetic acid on amylene was tried.

The amylene used was optically inactive and had a specific gravity of 0.6779 at 20° C. A mixture of equal volumes of amylene and glacial acetic acid had a specific gravity of 0.8639 at 20° C. immediately after mixing. A mixture of one volume of amylene and two volumes of glacial acetic acid had a specific gravity of 0.9250 at 20° C.

After standing for just one month the ester content was determined by means of a method similar to that used for the other mixtures.

1 Volume Amylene + 1 Volume Glacial Acetic Acid

Date	$(D)_{20^\circ}$	Ester No.	p. c. of ester	p. c. as ester
May 20, 1907................	0.864	12.86	2.97	7.90
1 Volume Amylene + 2 Volumes Glacial Acetic Acid				
May 20, 1907................	0.9253	7.97	1.85	7.58

CONCLUSIONS

In summarizing the facts brought out by the foregoing experiments one appears especially significant, namely the influence of the mass. In every experiment performed this is clearly brought out. The percentage of hydrocarbon changed to ester is, with one exception, appreciably higher in each case where the amount of the acid is doubled. In the curves accompanying these data, curve A shows in each case the results obtained from one volume of the hydrocarbon with one volume of the acid, and curve B the results obtained from one volume of the hydrocarbon with 2 volumes of the acid. A study of the curves will show that, with one exception, the percentage of the hydrocarbon changed to ester in mixture B is considerably higher than in mixture A. This increase in ester is apparent in the very first observation made and continues to be so throughout the entire time of observation extending through several months.

Whereas the amount of the acid in B in these experiments was only twice that in A, it is reasonable to suppose that a greater increase in the ratio of acid to hydrocarbon may lead to a still higher percentage of addition products formed. However, this has still to be proven experimentally. It seems safe to say, however, even from the few observations made in regard to the influence of mass action, that, to secure a yield of ester which would be of any practical commercial value, the significance of mass influence is a very important one, and one which will be deserving of careful consideration.

In the experiments with limonene not only the influence of mass action was observed, but also the influence of so-called catalytic agents. Anhydrous sodium acetate has long been employed in the acetylization of volatile oils by means of acetic acid anhydride. Just what its action is in such cases has never been satisfactorily explained. The fact remains, however, that it insures a more complete esterification. It was interesting, therefore, to try its action in these experiments, where we have ester formation, not by the action of an acid on alcohol as is supposed to be the case in volatile oils, but by direct addition. If in this case an increase of ester could be observed due to the presence of such a reagent then a similar significance might be attached to its use in the determination of alcohols in volatile oils.

Another so-called catalytic agent used was anhydrous hydrogen chloride. The mixtures of limonene and glacial acetic acid were exactly the same in each case and differed only in the presence of these so-called catalytic agents. Any difference in the percentage of hydrocarbon changed to ester can therefore only be accounted for by the action of these agents.

In studying the curves plotted from the data obtained from these experiments some extremely interesting results are brought out. The data thus far recorded have been obtained from observations extending over approximately five months. The first set of curves shows the amount of limonene changed to ester when standing in contact with glacial acetic acid alone. In five months a maximum of 2.84 p. c. was obtained. The second set of curves shows the influence of the anhydrous hydrogen chloride. In this case a maximum of 3.78 p. c. was obtained. The third set of curves shows the influence of the anhydrous sodium acetate. Here a maximum of 5.71 p. c. was observed. Thus we have a difference of 2.86 p. c. due to apparently no other cause than the influence of the sodium acetate, and an increase of 0.94 p. c. due to the influence of the hydrogen chloride. Thus with sodium acetate we have a percentage of ester which is a trifle more than twice that in a similar mixture but without the so-called catalytic agent. From these results it becomes evident that both the so-called catalytic agents used have a tendency to increase the additive capacity of the hydrocarbon, and that sodium acetate has by far the greater influence of the two. An interesting observation that should be made here is the relation of the presence of sodium acetate to mass action. It will be observed in the first two sets of curves that mixture B shows a considerable increase in percentage over A. In the curves for the mixtures containing sodium acetate, however, both show very nearly the same extent of ester formation. This is true throughout the entire period of observation. The influence of mass action is apparently lost here.

The experiments performed to show the influence of higher temperatures and pressure on the amount of ester formed bring out many points of interest. From the curves it can be seen that the greatest addition takes place during the first eight hours of heating. This is especially true where higher temperatures than 100° are employed. After heating 16 hours there is apparently little or no increase in the addition products formed; in fact in some cases there is a decrease as the curves indicate. In the mixtures containing one volume of pinene to two volumes of glacial acetic acid we practically reach the maximum percentage after the first eight hours of heating.

It must be borne in mind, however, that in these experiments we have entirely different conditions than in those where the time of contact alone becomes a factor. The high temperatures and the correspondingly high pressure under which these data were obtained doubtless give rise to reactions other than the mere addition of the acid to the ester-forming hydrocarbon. Thus there may be a change of the hydrocarbon pinene to its isomer limonene, or other similar reactions. The assumption that such varied, and possibly, highly complex changes take place under the existing conditions gains weight from the fact that the physical constants of these mixtures undergo extensive changes under this treatment. These changes seem to occur with no apparent regularity as is the case with the mixtures standing in simple contact at room temperature.

Viewed from a practical standpoint, it at once becomes apparent that there is no material advantage in prolonging the time of heating. From the data obtained thus far it seems safe to say that sixteen hours would be quite sufficient. As far as the change of the hydrocarbon to ester is concerned, the greatest efficiency is obtained by heating one volume of pinene with two volumes of glacial acetic acid at 175° to 185° for a period of about eight hours.

The experiments conducted with the object of determining the influence of increased pressure on the amount of ester formation have proved of very great importance. The results have demonstrated without doubt that any increase over normal atmospheric pressure and any temperature above the boiling point is of no material advantage. Thus the maximum percentage of hydrocarbon changed to ester at 175° to 185° is a trifle over 25 per cent after heating for 24 hours, while the maximum percentage obtained when boiling a similar mixture under ordinary pressure for 20 hours is 24.8 per cent. This result when viewed from a practical standpoint is of great significance. Whereas the last experiment is easily conducted, the first involves numerous technical difficulties, at least when conducted on a large scale.

One of the objects in view when these experiments were begun was to determine to what extent the amount of ester formation would be indicated by the physical constants. In the long series of observations on pinene with acetic acid some interesting points have been brought out in regard to the changes in physical constants. The changes were very gradual but after seven or more months of observation, it is found that the specific gravity has increased and the angle of rotation has decreased in both mixtures. With a few exceptions, due probably to experimental error, these changes have proceeded with fair regularity in both mixtures.

In the experiment with limonene we again find the specific gravity slowly increasing with the time of contact. This is especially true in cases where the so-called catalytic agents have been used. The optical activity, however, does not show any changes in any definite direction. In the experiments where higher temperatures and pressure are employed the physical constants, as has been mentioned previously, change back and forth without any regularity whatsoever. Taken as a whole the changes in the physical constants seem to be too small to serve as a valuable criterion in regard to the amount of ester present.

Finally, in summarizing the results which these experiments have brought out, it must become apparent that the matter under investigation is of sufficient interest, both practically as well as theoretically, to warrant a further systematic study of the subject. In the work here recorded only the action of acetic acid has been studied, but the investigation of the action of other organic acids appears fully as promising.

OBSERVATIONS AND CONCLUSIONS AFTER TWO AND ONE-HALF YEARS

The investigations recorded in the foregoing pages were temporarily brought to a close in June, 1907. The different mixtures of hydrocarbons and acids which had been used were carefully set aside to be examined again some time in the future, if the opportunity presented itself. Such an opportunity came in December, 1909, two and one-half years later. The mixtures were again examined as to specific gravity, angle of rotation, and the amount of esterification. The esters were determined in the same way as in the earlier examinations. In order to show the changes that had taken place in these mixtures since their last previous examination, the following tabulation is appended which shows the results of the last examination in 1907, and the recent one in December, 1909.

Pinene and Glacial Acetic Acid

Date	1 Vol. of Pinene + 1 Vol. of Acid			1 Vol. of Pinene + 2 Vols. of Acid		
	D_{20°	$(\alpha)_{20^\circ}$	p. c. of pinene as ester	D_{20°	$(\alpha)_{20^\circ}$	p. c. of pinene as ester
May 15, 1907...	0.9502	+7° 18′	7.40	0.9804	+4° 15′	9.05
Dec. 7, 1909....	0.9590	+3° 15′	18.30	0.9960	+2° 15′	28.70

LIMONENE AND GLACIAL ACETIC ACID

Date	1 Vol. of Limonene + 1 Vol. of Acid			1 Vol. of Limonene+2 Vols. of Acid		
	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester.	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester.
May 15, 1907.	0.9400	+47° 0′	2.06	0.9748	+31° 43′	2.74
Dec. 7, 1909.	0.9470	+38° 39′	12.90	0.9680	+28° 42′	10.07

LIMONENE AND GLACIAL ACETIC ACID AND ANHYDROUS HYDROGEN CHLORIDE

Date	1 Vol. of Limonene + 1 Vol. of Acid + 1.11 gms. of H Cl.			1 Vol. of Limonene + 2 Vols. of Ac. + 1.11 gms. of H Cl.		
	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester
May 15, 1907.	0.9408	+46° 45′	2.78	0.9754	+31° 25′	3.78
Dec. 7, 1909.	0.9430	+46° 16′	7.47	0.9770	+30° 20′	9.39

LIMONENE AND GLACIAL ACETIC ACID AND ANHYDROUS SODIUM ACETATE

Date	1 Vol. of Lim. + 1 Vol. of Acid + 2.5 gms. of Na $OCOCH_3$			1 Vol. of Lim. + 2 Vols. of Acid + 2.5 gms. of Na $OCOCH_3$		
	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester	$D_{20°}$	$(\alpha)_{20°}$	p. c. limonene as ester
May 15, 1907.	0.9490	+45° 15′	5.19	0.9798	+31° 12′	5.70
Dec. 7, 1909.	0.9709	+35° 45′	33.39	0.9870	+28° 58′	15.95

AMYLENE AND GLACIAL ACETIC ACID

Date	1 Vol. of Amylene + 1 Vol. of Acid			1 Vol. Amylene + 2 Vols. Acid		
	$D_{20°}$		p. c. amylene as ester	$D_{20°}$		p. c. amylene as ester
May 20, 1907.	0.9640	....	7.90	0.9253	....	7.58
Dec. 7, 1909.	0.9560	....	23.00	0.9910	....	33.80

Taken as a whole the changes which have taken place in these mixtures in the last two and one-half years have been largely in the direction indicated by the observations made during the first five months. In the mixtures of pinene and glacial acetic acid the specific gravity has continued to increase very gradually while the angle of rotation has decreased to about one-half in both mixtures. The amount of esters has also very materially increased.

In the mixtures of limonene and glacial acetic acid similar changes as indicated in the pinene mixtures have taken place but to a much smaller extent. In those mixtures containing hydrogen chloride as a catalytic agent the changes, though in the same direction as indicated previously have been very small indeed. A much higher formation of esters and a correspondingly greater change in the physical constants has taken place in the mixture of limonene and acetic acid containing anhydrous sodium acetate. This is especially true where equal parts of acid and hydrocarbon are used. It seems that here the catalytic action of the sodium acetate has exerted a very strong influence. The mixtures of amylene and acetic acid show a very considerable increase in specific gravity and a large amount of ester.

In commenting on the results obtained in the first few months, attention was directed to the apparent influence of mass action. The extent of ester formation was in almost every case greater where the amount of the acid was doubled. This influence of mass action is much less evident after the recent examination. Yet it remains apparent in the mixtures of pinene and acetic acid, in the mixtures of limonene and acetic acid with the anhydrous hydrogen chloride, and in the mixtures of amylene and acetic acid. On the other hand in the case of limonene and acetic acid and limonene and acetic acid with the anhydrous sodium acetate the indication is in the opposite direction. The latter mixture, even during the first five months showed that the amount of ester formed, where the volume of acetic acid was doubled, was practically the same as where equal volumes of the acid and limonene were used. Now, after a much longer period of contact it is found that the mixture of equal volumes shows 33.3 p. c. of limonene changed to esters and the mixture where the acid was doubled only 13.95 p. c. In these same mixtures the higher per cent of esterification is accompanied by a correspondingly greater change in the physical constants. It seems then that nothing definite can be said about the influences of mass action, especially in mixtures containing limonene to which catalytic agents have been added. On the other hand, in mixtures of pinene and also those of amylene the effect of mass action seems to be quite clearly indicated.

The physical constants show, on the whole, very consistent changes. The specific gravity has steadily increased in all cases and the angle of rotation decreased. It is also seen that in the majority of cases, and this is especially true of the angle of rotation, the extent of the change is largely in proportion to the amount of ester formed.

REVIEW OF LITERATURE

Bouchardat et Lafont, 1886. Sur Une Nouvelle Synthèse D'un Bornéol Inactif. Compt. Rend., 102, p. 171

A mixture of one part of turpentine oil and one and one-half parts of glacial acetic acid was heated for 36 hours at 100°. The mixture was agitated with water, then with a solution of an alkali and finally submitted to fractional distillation. The products of the distillation were: pinene boiling at 156° and another product boiling at 215°. Under the above conditions only a small amount of pinene is combined. If the mixture is heated to 150° the reaction is greatly increased, and a substance boiling at 215° is obtained. This is the acetic ester of borneol. It is a white mobile liquid with an odor reminding of thyme, optically inactive, with a specific gravity of 0.977 at 0° C. Upon heating for six hours in a sealed tube with alcoholic potassa it is saponified and inactive borneol is formed.

Bouchardat et Lafont, 1886. Sur L'action de l'acide Acétique Sur L'essence de Térébenthine. Compt. Rend., 102, p. 318. [Jour. Chem. Soc., 50, p. 475.]

In the experiments performed with pinene and acetic acid the following facts were brought out:

Acetic acid combines with pinene in the cold forming the monoacetates, belonging to two distinct series. At the same time the pinene not combined is changed to two isomeric hydrocarbons $C_{10}H_{16}$, one "monovalent," i. e. "térébenthène," with one double bond; and the other "bivalent," i. e. "terpilène," with two double bonds.

Bouchardat et Lafont, 1886. Formation D'alcools Monoatomiques Dérivés de L'essence de Térébenthine. Compt. Rend., 102, p. 433

From French turpentine two acetates were obtained with the same empirical formulas, $C_{10}H_{16}(C_2H_4O_2)$, but with widely different properties. From these acetates the two corresponding alcohols were obtained. Both alcohols have the formula

$C_{10}H_{18}O$, but their properties are totally different. The method of obtaining the acetates was as follows: The mixture of the compounds resulting from the turpentine oil and acetic acid was warmed with its weight of potassa and five or six times its weight of alcohol in a sealed tube at 100°C. for 10 hours. Upon the addition of water an oily layer separated which was purified by redistillation.

The following tabulation shows the acetates that were obtained and the products which they yielded upon saponfication:

Acetate formed	B. P.*	$(\alpha)_D$	Alc. formed on saponification	B. P.*	(α)
$C_{10}H_{16}(C_2H_4O_2)$..........	95-105°	+ 1° 16′	Terpilenol.....	99-102°	—17° 24′
Acetate de térébenthine....	105-110°	....	Terpilenol camphenol...	....	—43° 6′
Acetate de terpilène........	110-116°	....	Terpilenol.....	99-105°	Active

* Under diminished pressure, "dans le vide."

From the alcohol obtained from the first acetate in the table a crystalline substance separated which was dried on porous plate. It was found to be laevogyrate borneol. It is observed that there is a more abundant production of laevogyrate borneol than of dextrogyrate borneol.

Lextrait. Action de L'acide Picrique Sur le Térébenthène, et sur le thymène. Compt. Rend., 102, p. 555 [Ber. 19, p. 237, Ref.]

Picric acid does not act on pinene or oil of turpentine in the cold, but at 150° vigorous action sets in. Upon cooling, yellow crystals separate which can be washed with hot alcohol. These crystals have the formula: $C_{10}H_{16}C_6H_2(NO_2)_3OH$. The crystals are insoluble in water but soluble in boiling alcohol and ether. Upon boiling with caustic potash they yield borneol as a white precipitate. This borneol has a melting point 199°-200° and boils at 211°; $\alpha_D = —37°$. With HCl it gives a compound decomposible by boiling water; and with nitric acid a substance which corresponds with ordinary camphor in odor, composition, boiling and melting point.

Bouchardat et Lafont, 1891. Action de L'acide Benzoique Sur L'essence de Térébenthine. Compt. Rend., 113, p. 551

Benzoic acid acts slowly on turpentine oil in the cold. Upon heating to 150° the reaction is more rapid. After heating for 50 hours all the oil is changed. It is best not to let the temperature go much above 150°. The operation is best carried out by heating in a copper vessel with a reflux condenser.

The products formed are numerous. Any excess of acid is taken out with an alkaline solution. It is then distilled up to

It is supposed that the benzoate of pinene is first formed which upon the prolonged heating decomposes into camphene and terpilene.

200°–220°. The products of the fractionation are:

1. Camphene $\alpha_D = -3°30'$ b. p. 157°
2. Terpilene $\alpha_D = -3°$ to $4°30'$ b. p. 175°–180°

Tilden and Forster, 1893. Preparation of Bornyl Picrate. Journ. Chem. Soc., 1893, 1, p. 1388. [Ber. 37, p. 136, Ref.]

Picric acid is heated with ten times its weight of pinene to 150°. The reaction keeps the temperature up. Some water is produced and some of the acid changes to a tarry mass. When the excess of the acid begins to solidify the dark brown liquid is decanted into a beaker and after several hours tufts of yellow crystals form. These are washed with cold alcohol, and then crushed with water in a mortar as long as the latter turns yellow. They are then recrystallized several times from hot alcohol; m. p. 133°.

The picrate obtained from American turpentine oil was identical with that obtained from French turpentine. The latter yielded a borneol which was leavo, while the former yielded an inactive borneol. When the picrate was heated alone a distillate was obtained which solidified and was found to be camphene; m. p. 47°.

Bouchardat et Tardy, 1895. Sur les Alcools Dérivés d'un Térébinthène droit, L'eucalyptène. Compt. Rend., 120, p. 1417.

Voiry has made known the presence of small quantities of a strongly dextrogyrate terpene in the oil of *Eucalyptus globulus* distilled in France. This terpene, after numerous rectifications, had an optical rotation of +34°10′ in a 100mm tube. The terpene obtained from the same species of Eucalyptus but from a different province was almost entirely inactive. This terpene is considered to be a mixture of a dextro and a levo terpene which makes it entirely or almost entirely inactive. A terpene, -40°30′, was transformed into terpineol formate by acting on it with crystallized formic acid in the cold. This was then saponified and upon distillation yielded an oil which solidified in a freezing mixture. The terpineol m. p. 33°–34° thus prepared has all the properties of that obtained from laevo-pinene.

Borneol and iso-borneol were prepared from this "eucalyptene" by heating with benzoic acid to 150°. Most of the terpene is changed to dextro limonene. Another part formed the benzoic ether of a dextro borneol and of the optical isomer isoborneol or fenchol. The dextro borneol obtained in this method possessed optical peculiarities but rarely observed by the author in connection with the other synthetic borneols. Its melting point, after numerous crystallizations from petroleum ether and carbon disulphide, was in the neighborhood of 213°. Its angle of rotation was +18°40′ whereas that of the camphor which it yielded was +31°.

The fenchol or iso-borneol obtained was separated by a series of distillations and crystallizations Its m. p. was 45° and b. p. about 198°–200°. It has all the properties of iso-borneol prepared from laevo pinene. It furnishes a d-camphor upon oxidation which is liquid at 15°, solid at 0°. It is strongly dextrogyrate and seems to be identical with anise camphor of Landolph or the fenchone of Wallach.

Kriewitz, O., 1899. Ueber Addition von Formaldehyd an enige Terpene. Ber., 32, p. 57

Twenty gms. of the pinene fraction of American turpentine oil, 4.4 gms. of paraformaldehyde and 10 gms. of alcohol are heated in a sealed tube to 170°–175° for about 12 hours. After cooling water is added and an oily layer separates which is shaken out with ether. Upon fractionation a large quantity of turpentine comes over. Fraction 225°–240° is rectified with steam. The oily distillate is shaken out with ether and after the evaporation of the ether the oil remaining is fractionated and fraction 232°–236° is collected. It is a clear liquid of a somewhat thick consistance with an oder reminding of turpentine. It is insoluble in water but soluble in ether, alcohol, and ligroin. It is very hygroscopic, strongly dextrogyrate, and has a specific gravity of 0.9610 at 20°C. The yield is very small, being only about 15 per cent. of the pinene used. The compound was found upon analysis to have the formula $C_{11}H_{18}O$. It adds two molecules of hydrogen chloride, hence is unsaturated. That an alcohol group results is revealed by the formation of an acetyl and a benzoyl compound.

Dextro limonene and dipentene form similar addition products with formaldehyde.

Wallach, O., 1901. Reobachtungen in der Fenchen Riehe. Ann. 315, p. 273

Mix 20 gms. of fenchene with 40 gms. of alcohol and 7 cc. of dilute sulphuric acid and heat it on a water bath for some hours. Only a small quantity of fenchene is recovered and in its place a number of higher boiling compounds are formed. Fraction 200°–201° was found to have the formula $C_{10}H_{17}OC_2H_5$ or ethyl ether of iso-fenchyl alcohol.

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THE MONARDAS

A PHYTOCHEMICAL STUDY

BY

NELLIE WAKEMAN

Assistant in Pharmaceutical Chemistry
The University of Wisconsin

CONTRIBUTIONS FROM THE COURSE IN PHARMACY

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THE GENUS MONARDA

History.[*] This interesting plant, which seems to be a strictly American genus, and which is national if not continental as to its range and habitat, including as it does, species adapted to all locations and all conditions of soil and climate from ocean to ocean, and from beyond the Great Lakes to the Gulf of Mexico, has probably been known and admired as long as this continent has been inhabited. It does not seem possible that its gaily colored blossoms and pleasant aromatic odor could have escaped the notice of the early white settlers, while it is highly probable that the same qualities recommended it to the aborigines as an ingredient for their medicine bags. Of the many species of *Monarda* at least three were early put to economic uses. *M. fistulosa* was used as a febrifuge;[1] *M. punctata* as an emmenagogue and as an antispasmodic to relieve the nausea which attended the bilious fevers of America; and the leaves of *M. didyma* were dried and made into a tea which was used as a beverage in place of the expensive Chinese tea.[2] Indeed, so prevalent was the use of *M. punctata* as a medicinal plant that it was made official in the first American Pharmacopoeia [3] and it remained among the official plants until 1870.

Concerning the early use of the Monardas in medicine, Professor Lloyd has kindly furnished the following information.

"Briefly, the therapeutic record of Monarda begins with its employment by the Indians near Lake Oswego, from which circumstance it obtained the name, *Oswego Tea.* It was thus introduced to the Botanics of an early date, who employed it in decoctions and infusions. Thence, Schoepf, Barton, Rafinesque, Atlee, and other writers gave it more or less extended notice. The abundance of its oil led to its early distillation, and to the use of this oil in domestic medicine, as a liniment. The essay of Dr. Atlee,[4] published in 1829, in which he made extravagant claims for the drug, introduced the oil conspicuously to the profession, since which date the record of Monarda has been that of other medicinal plants."[5]

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[*] Thanks are due Professors J. U. Lloyd of Cincinnati and Wm. Trelease of St. Louis for making available for this chapter information from the books of the collections of the Lloyd library and the Shaw School of Botany.

[1] Redwood—*Supplement to the Pharmacopoeia,* p. 433 (1857). Also Gray. *Treatise on Pharmacology,* p. 48. (1836) .

[2] *Jr. de Ph. et de Chim.,* 7, p. 89. (1815)

[3] *U. S. P.,* 1820, p. 55.

The genus *Monarda* was named in honor of Nicholas Monardes,[6] a physician of Seville, who wrote many tracts upon medicinal and other useful plants, especially those of the New World, in the latter half of the sixteenth century. That Monardes in any way described the genus *Monarda* is doubtful, and it has not yet been ascertained to whom shall be accorded the credit of naming the genus, though it is usually ascribed to Linnaeus, no record having been found of the use of the name Monarda before he, in his *Genera Plantarum,* of 1737, published it. That Linnaeus was not, however, the first to describe the plant becomes apparent from the fact that Cornuti [7], in 1637, mentions *Monarda fistulosa* in his enumeration of North American plants in his "*Plantarum Canadenseum.*" He, however, called it *Origanum fistulosum Canadense.*[8]

ORIGANUM FISTULOSUM

Canadense

CAP VI

Frvticosa & cubitalis herba è Canada nuper aduenit, quam Origanum Fistulosum nominauimus: quod tubuli floris ita sint inter se compositi, vt quandam velut cicutis compactam Fistulam repraesentent. Caulibus exit quadratis, nunc angulosis, sub hirsutis, & ramosis. Foliis longis, Lysimachiae siliquosae aemulis, dilutè virentibus, quae ab imo ad caulis fastigium vsque pullulant, ibique minora decem aut duodecim in orbem congesta floris obambiunt globum, qui Scabiosae capitulum refert (quamuis sit latior multoque depressior:) mille caliculis conflatur, à quibus funduntur ordinatè dispositi tubuli plures, semiuncialis

---

[4] Essay of Dr. Atlee, *Medical Recorder* (1829).

[5] Professor Lloyd apparently does not distinguish between the early history of *M. didyma* which, because of its exceedingly low oil content, was used as a tea, and that of *M. punctata* which, because of its relatively high oil content, was used for medicinal purposes.

[6] Don's *Gardener's Dictionary*, Vol. 4, p. 758. (Benth. Labitarum genera et species, p. 315.) Also Gray's *New Manual of Botany* (1908), p. 703.

[7] Cornuti, *Canadenseum Plantarum Historia* (1635) pp. 13-15; also Pickering *Chronological arrangements of plants*, p. 948; from Sprengel und Winckler.

[8] Cornuti, *Can. Plant. Hist.* (1635), pages 13 to 15 under the name of Origanum Fistulosum, Canadense, pictures and describes Monarda Fistulosa.

In 1705, according to Pickering, Plukenet[9] designates it *Monarda* punctata in his *Amaltheum*. If Plukenet himself called the plant *Monarda punctata* the credit for naming the genus can not, certainly, go to Linnaeus, for this was about the time of the birth of the great naturalist. Whether this is so, or whether the plant was described under some other name and identified as *Monarda punctata* by Sprengel and Winckler, whom Pickering quotes as authority, can be decided only by referring to the original literature. In 1737, however, Linnaeus[10] mentions *M. didyma* in his "Hortus Cliffortianus,"[11]

---

longitudinis, coloris ex purpurâ colossini, bifidi extremo quo patentem rictum fingunt, vnde profluunt duo aut tria cum purpureis apicibus filamenta. Prolifera est, caulem enim saepe trans'lit caulis, qui tribus digitis à primo flore eleuatus, subiectis totidem foliolis, novo floris alterius globo repullulat. Tota planta caulibus atque adeo folijs subincana lanugine pubescit. Efflat odorem non trita Satureiae hortensis. Sapor huic acerrimus, ac Hydropiperis more linguam peruerns, exceptâ radice quae foliis contexitur fibris: haec namque nescio quo naturae lusu, prorsus insipida gustanti percipitur. Floret Iulio & Augusto mensibus: Huius vita in multos annos protrahitur ópcyaros Graecis, quasiō plor yáros montanum gaudium dicitur.—From a letter from Professor Trelease.

[9] *Ibid.* p. 999: from Sprengel and Winckler.

[10] Linnaeus, *Hortus Cliffortianus* (1731) pp. 11, 12, Appendix of species, p. 495; also Pickering. p. 1015; from Sprengel und Winckler.

[11] In his Hortus Cliffortianus, of 1737, Linnaeus says of the genus:

"MONARDA, g. pl. 17

1. Monarda.

Origanum spurium, flore Fistuloso. *Riv. mon.* 89.
Origanum fistulosum canadense. *Corn. canad.* 13. f. 14. *Raj. hist.* 380.
Leonurus canadensis, origani folio. *Tournef. inst.* 187.
Clinopodium canadense majus hirsutius, floribus fistulosis. *Moris. hist.* 3. p. 374, s. 11. t. 8. f. 2.
Clinopodium canadense fistulosum, foliis lanuginosis, proliferum. *Pluk. alm.* 111.
Clinopodium canadense fistulosum foliis dilute virentibus & hirsutis. *Boerh. lugdb.* 1. p. 158.
Clinopodium canadense fistulosum, foliis saturatius virentibus & hirsutis. *Boerh. ludgb.* 1. p. 158.
Crescit in Canada, *heic verbo-hyemes perfert.*

Nomen obtinuit planta haec capite crasso a Monardo *utroque quorum alter in conquirendo quidquid salutare ex novo orbe ferunt plantae, quidquid sub* Rosis & Citris *obtulit natura; alter vero perquirendo veterum scripta, orbi satisfacere studuit."* (pages 11 and 12).

In an appendix of species (page 495) of the same work he says further:

"2. MONARDA floribus verticillatis.

Clinopodium virginianum angustifolium, floribus amplis luteis purpuro—maculatis, cujus caulis sub quovis verticillo decem vel duodecim foliolis rubentibus est cinctus. *Pluk. alm.* 111, t. 24, f. 1.
Crescit in Virginia.
Cum haec Monardae sit species dicatur praecedens (spec. 1).
Monarda capitulis terminatricibus, caule obtuse angulato; *cum alia datur species inter virginianas D. Gronovii* caule acute angulato, capitulisque terminatricibus."

—From a letter from Professor Trelease.

where he also describes the genus, giving references to Cornuti, Plukenet, Tournefort, and other earlier writers. These three references appear to be the first in which the *Monarda* species, viz. *fistulosa, punctata,* and *didyma* are mentioned in botanical literature.

DISTRIBUTION OF SPECIES. According to Engler and Prantl,[1] *Monarda* is a North American plant and consists of about 18 species distributed over the southern part of North America; in the East from New Brunswick and Ontario to Florida and Louisiana, and in the west from British Columbia to New Mexico, Arizona and Texas.

Owing to the fact that in many instances the same species has been described by different authors under different names; and that often what has been considered as a variety of a species by one botanist has been described as a distinct species by another, and vice versa, there is a confusion of names that bewilders the non expert at botanical classification so that the 18 species of Engler and Prantl appear as 50 or 60. Without attempting, therefore, a complete classification of the species and varieties of the genus *Monarda,* a task which is clearly not that of the plant chemist, the following list has been compiled. This attempt to harmonize the descriptions of the best authorities seemed necessary for a rational biochemical treatment of the genus and for securing the desired material. It is to be hoped that a botanist will soon place this genus on a better basis systematically.

Botanical Name	*Common Name*	*Distribution*
M. albiflora, Morr.		
M. Beckii, Eaton Man.		
M. Braaburiana, B.		Indiana to Tennessee and Missouri.
M. amplexicaulis, Fisch.		
M. fistulosa, Hook.		
M. villosa, Martens.		
M. citriodora, Cerv.	Lemon mint.	Ill. to Neb. and Texas.
M. Aristata, Nutt.	Prairie bergamot.	
M. clinopodia, L.		Ontario to Georgia and Kentucky.
M. Altissima, Willd.		
M. glabra. Lam.		

---

[1] Engler und Prantl—*Die Natuerlichen Pflanzenfamilien.* Vol. 4. Part 3a, p. 289.

Botanical Name	*Common Name*	*Distribution*
M. rugosa. Ait.		
M. cliropodioides, A. Gray.		Texas. Southern Kansas.
M. contorta, Morr.		Colorado (to 8000 ft)
M. comata, Ryd.		
M. didyma, L.	Oswego tea	New Brunswick to
M. coccinea. Michx.	American bee balm	Ontario and Mich.
M. didynama, Stokes	Fragrant balm	South to Georgia.
M. fistulosa, Curt.	Mountain mint.	
M. Kalmiana, Pursh.	Indian plume	Ascends to 5200 ft.
M. Oswegoensis, Bart.		in N. Carolina.
M. purpurea, Lam.		
M. dispersa, Small.		Fla. Ga. Tex. Mex.
M. fistulosa, L.	Wild bergamot	New England to
M. allophylla, Michx.	Balm	Colorado and Texas.
M. barbata, Wender.		
M. coerulea, Hort ex-Benth.		
M. dubia, Hort ex-Benth.		
M. elongata, A. Dietr.		
M. hybrida, Wender.		
M. involucrata, Wender.		
M. Lindheimeri, Engelm & Gray.		
M. longifolia, Lam.		
M. media, Willd.		
M. menthaefolia, R. Grah.		
M. mollis, Linn.		
M. oblongata. Ait.		
M. purpurascens, Dum. Cours.		
M. purpurea, Pursh.		
M. scabra, Beck.		
M. undulata, Bart.		
M. violacea, Desf.		
M. virginalis, Hort.		
M. fistulosa, var. media. Willd.		Maine to Virgina along mountains.
M. media, Willd.		
M. fistulosa, var. mollis, Benth.		New England to S. Dak. and Texas.
M. mollis, L.		
M. scabra, Beck.		N. W. Ter. & Brit. Col. to Mo. Tex. and Ariz.
M. hirsutissima, Small.		Texas.
M. lasiodonta, (Gray) Small.		Tex. Ariz. Oklahoma, Colo. Utah
M. menthaefolia, Benth.		N. Mex. Manitoba to Tex.
M. pectinata, Nutt.		and New Mexico.

M. penicillata, A. Gray.		
M. pratnsis, Rafin.		
M. punctata, L.	Horse mint	N. Y. to Minn.
M. lutea, Michx.		South to Fla. & Tex.
M. Ramaleyi, A. Nels.		Colorado.
M. rigida, Rafin.		
M. Russeliana, Nutt.		Ark.
M. Stanfieldii, Small.		Oklahoma & Texas.
M. Stricta, Wooten.		Wyoming to N. Mex.
M. tenuiaristata (Gray) Small.		Kan. to Ark. & N. Mex.
M. Virgata, Rafin.		

The above list was compiled with the aid of Professor R. H. Denniston of the University of Wisconsin, and submitted to the criticism of Mr. Moses Craig of the Missouri Botanical Garden.

REVIEW OF THE CHEMICAL WORK ON THE MONARDAS

GENERAL STATEMENT. The earliest record that we find of chemical work upon any of the *Monarda* species is that of Elsner,[1] who, in 1832, in the course of a rather extended series of observations upon the red coloring matter of flowers, extracted the red pigment from *M. coccinea* (*M. didyma*) and tested it with various reagents. By whom and when the oils were first distilled from these plants we have no knowledge. The first mention that we find of the oils in chemical literature is Procter's[2] report, in 1845, of the occurrence of a crystalline product in the volatile oil of horsemint. He compared the appearance of this crystalline mass with camphor and called it monardin. The next year Arppe[3] made a similar report upon the stearopten which Flueckiger[4] in 1884 identified as thymol.

In 1888 Schroeter[5] made an examination of three samples of oil, supposed to have been obtained from *M. punctata*, separating it, as had Arppe forty years earlier, into "thymol" and a liquid portion. Schroeter's description of the low melting point of the "thymol" obtained, and of its dextro rotary power aroused suspicion in the minds of chemists in this laboratory and invited further investigation. Accordingly, in 1894, *M. fistulosa*[6] was collected and distilled and a chemical study made of the oil. During the following summer a similar study was made of the oil derived from *M. punctata.*[7] From these preliminary studies it was learned that while the oil from *M. punctata* contains thymol, that from *M. fisulosa* contains the isomeric phenol, viz. carvacrol.

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[1] *Chem. Centralb.*, 3, p. 571.
[2] *Am. J. Ph.*, 17, p. 86.
[3] *Ann.*, 58, p. 41.
[4] *Ber. Sch. & Co.*, Sept., '84, p. 12.
[5] *Am. Jr. Ph.*, 60, p. 113, 149.

Up to the present time *M. punctata* and *M. fistulosa* have been investigated repeatedly in a number of directions. However, efforts have also been made to secure species not found in this vicinity. As a result, *M. didyma* and *M. citriodora* have been subjected to preliminary examinations.

The more detailed investigation of *M. fistulosa* led to the discovery of a red crystalline substance originally believed to be alizarin-like in character. This, together with other observations made on the color of the stems and of the oils early directed attention to pigmentation. The later discovery of hydrothymoquinone[8] and thymoquinone[9] led to the quinhydrone hypothesis of plant pigmentation.

The assumption that the plant oxidises thymol or carvacrol to hydrothymoquinone, then to thymoquinone, and, as has since become apparent, to higher oxidation products, naturally led to the inquiry "what is the mechanism by which the plant accomplishes this oxidation?" This inquiry invited to a study of the oxidases[10] of these plants and their action upon the chemical constituents of the Monardas.

Inasmuch as the color of the quinhydrone is materially influenced by metals and their salts, an insight into the inorganic components of these plants became a necessity. So, step by step, from the simple examination of a single volatile oil has grown a phytochemical study of a genus of plants and of the biochemical activities of its specific representatives.

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[6] *Ph. Rund.*, 13, p. 207.
[7] *Ph. Rev.*, 14, p. 223.
[8] *Ph. Rev.*, 19, p. 244.
[9] *Ph. Rev.*, 19, p. 200.
[10] *Ph. Rev.*, 22, p. 190.

MONARDA CITRIODORA.[11] During the summer of 1903 about 50 lbs. of the flowering herb of *M. citriodora* were collected near Dallas, Texas, and distilled in this laboratory, yielding about 200 gms. of oil. This oil was examined by Brandel[12] and found to contain carvacrol and hydrothymoquinone, while the presence of thymoquinone, thymoquinhydrone and possibly citral was indicated. This seems to have been the first chemical examination of the oil from this species.

A larger amount of oil, about 500 grams, was obtained in the summer of 1905 but was lost during the process of moving to the new laboratories.

In 1908 Le Febre[13] made an examination of two relatively small samples of oil, the one distilled in 1904, the other in 1907. He determined the amounts of phenol and aldehyde present.

MONARDA DIDYMA. It is not surprising that, on account of the brillant red of its blossoms as well as the rich tinting of its upper leaves, *M. didyma* should have early attracted the attention of chemists who were interested in plant pigmentation. The remarkable fact is that, after more than three-fourths of a century of rapid advance in chemical knowledge, we have as yet no proof positive of the composition of the substance or substances that impart the beautiful red color. It was Elsner,[14] who, in 1832, made what appears to have been the first chemical study of any of the Monardas. The record of his work is brief. He simply states that the dried "Farbstoff" is of a beautiful purple-red color and that it gives a bluish-green precipitate with basic lead acetate and a violet red precipitate with normal lead acetate. Interpreted in the light of our present knowledge of the pigments of the Monardas, these reactions seem to indicate the presence of monohydroxy and dihydroxy thymoquinone, since the monohydroxy compound gives the violet-red and the dihydroxy compound the green color reaction with both salts.

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[11] The material used in the study of this species was obtained at first through the kindness of the late Mr. Reverchon and later through the kindness of Mr. E. G. Eberle of Dallas, Texas.

[12] *Ph. Rev.*, 22, p. 153.

[13] *Mid. Drug. Ph. Rev.*, 44, p. 526.

[14] *Chem. Centrabl.*, 3, p. 571.

In 1856 Belhomme,[15] who, like Elsner, was attracted by the color of the flower made a study of *M. didyma*. He obtained an extract of the blossoms and satisfied himself by its behavior toward various reagents, that the beautiful color is due to carmine, identical with that obtained from the cochineal insect. Belhomme thought that since the plant flowers freely, this discovery of a vegetable source of carmine might prove of great value to the silk industry. His hopes in this respect were not realized any more than his suppositions as to the identity of the pigment were verified.

It was nearly half a century later (1903) when Brandel[16] distilled 100 pounds of "Oswego tea" and examined the oil of which a yield of only about 0.03 per cent was obtained.

With only this small amount of oil to study, the results were necessarily meager. Nor do Schimmel and Co.,[17] who report upon the oil of *M.didyma* in 1908 and again in 1909, give much more than the physical constants. While the plant can scarcely be called rare, the yield of oil is so small that almost nothing is known of the chemical composition of the oil from this fragrant, most beautiful and, in many respects, most interesting of the Monarda species.

In Brandel's[18] monograph on "Plant Pigments" (1908) he characterizes the color of the flower of *M. didyma* as purple, and states that the alcoholic extract from the blossom is colorless, yielding upon evaporation a red residue. This would indicate that the pigment of this species belongs to the class of quinhydrones.

The fact, however, that the flowers of *M. didyma* are deep cardinal in color and that the alcoholic extract from the blossoms collected in the experimental gardens of the University is bright red, pink even in dilute solutions, leads to the supposition that possibly some error has crept into the identity of the material used.

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[15] *Compt. Rend.*, 43, p. 382.
[16] *Ph. Rev.*, 21, p. 109.
[17] *Mid. Drug. Ph. Rev.*, 44, p. 526.
[18] *Ph. Rev.*, 26, pp. 67 and 121.

MONARDA FISTULOSA. The first study of *M. fistulosa* from authentic material was an examination, in 1894, of oil distilled from flowering plants growing near Madison. This oil was examined by Mead and Brennan.[19] Carvacrol and cymene were identified while the presence of other substances, which could not be identified at that time was indicated. Among these was a red crystalline substance, described as alizarin-like, which was believed to impart the red color often found in the crude oils.

Work upon the oil of *M. fistulosa* was continued in this laboratory by Brandel[20] and others. In 1901 thymoquinone and hydrothymoquinone together with thymoquinhydrone, were isolated from the oil. The discovery of these substances immediately suggested an explanation for the purple color of stem and flowers; also for the spontaneous coloration of the monarda oils upon standing. It was in this connection that the quinhydrone hypothesis of plant pigmentation suggested itself.

The presence of hydrothymoquinone and thymoquinone, oxidation products of thymol and carvacrol, in monarda oils led to the question: What is the means by which the plant accomplishes this oxidation? The next step, therefore, was an examination of the plant to ascertain the presence of oxidases, and Rabak[21] (1904) found in *M. fistulosa* an oxidase which oxidises hydrothymoquinone to thymoquinone with the formation of the highly colored quinhydrone as an intermediate product. The study of oxidases in the monardas was continued by Swingle 1904)[22] who determined the thermal death point of the ferment; also by the writer[23] (1907) who determined quantitatively the amount of the oxidase in different parts of the plant and at different stages of growth.

During the winter of 1906-07 Suzuki,[24] while distilling with steam the phenol portion of an oil obtained from *M. fistulosa*, again obtained the red crystals, which separated on the inner wall of the condenser as before.

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[19] *Ph. Rund.*, 13, p. 207; also *Proc. A. Ph. A.*, 43, p. 256.

[20] *Ph. Arch.*, 2, p. 76; *Ph. Rev.*, 14, p. 198; vol. 15, p. 86; vol. 19, pp. 200 and 244.

[21] *Ph. Rev.*, 22, p. 190.

[22] *Ph. Rev.*, 22, p. 193.

[23] *Ph. Rev.*, 26, p. 314.

[24] *Unpublished manuscript.*

When purified by recrystallization from hot alcohol, these crystals (m. p. 226°), compared originally with alizarin, were found to resemble it in some respects while differing from it completely in others.

That the red crystalline product was possibly derived from the carvacrol in which it had been dissolved before distillation, seemed reasonable to suppose. Therefore a study of the oxidation products of thymol and carvacrol—hydrothymoquinone, thymoquinone, and the hydroxythymoquinones—was undertaken by the writer[25] (1908 and 1909), a study which resulted in the identification of the red crystals with dihydroxythymoquinone.

MONARDA PUNCTATA. The oil of horsemint was the first of the monarda oils to be prepared and examined chemically. As already stated, Procter,[26] in 1845, called attention to the crystalline, camphor-like product deposited in the volatile oil of horsemint. This deposit which was evidently thymol, Procter called monardin. While he made no chemical study of the substance he recorded its melting point as 118° F (48° C) and its boiling point as 413–418° F (211.5° C).

A year later, 1846, Arppe[27] examined a specimen of the oil of horsemint and separated the crystalline stearoptene. An elementary analysis gave C=80 per cent, H=9.52 per cent, O=10-.48 per cent. Arppe's work was confined mainly to a study of the physical properties of the stearoptene. He gives m. p. 48°, b. p. 220° C.

Although we have here two accounts of the separation of the stearoptene from the liquid portion of the oil, the crystalline product was probably not recognized as a phenol till Flueckiger[28] in 1884 identified it as thymol. The year following, the chemists of Schimmel & Co.[29] announced that the oil from horsemint contains 20–30 per cent of thymol.

In 1888, Schroeter[30] examined three specimens of oil supposed to have been derived from *M. punctata.* One of these was an old cabinet specimen and contained a crystalline deposit of thymol, the others gave no such deposit until subjected to a temperature of -15°. These evidently contained carvacrol, and the oil, which was not obtained from an authentic source, was probably *M. fistulosa.*

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[25] *Ph. Rev.*, 26, pp. 329, 364:
[26] *Am. Jour. Ph.*, 17, p. 86.
[27] *Ann.*, 58. p. 41.
[28] *Ber. S. & Co.*, Sept., '84, p. 17.
[29] *Ber. S. & Co.*, Sept., '85, p. 20.
[30] *Am. Jr. Ph.*, 80, p. 113.

The first work, however, with authentic material was that of Schumann[31] in 1896, who distilled the oil from *M. punctata* collected near Pine Bluff, Wisconsin, and identified by Professor L. S. Cheney, then of the University of Wisconsin. This oil upon examination was found to contain thymol to the extent of more than 50 per cent, cymene, and some oxygenated non-phenol compound. Another examination of oil distilled from plants collected at Arena, Wisconsin, gave similar results, as did also an oil distilled by W. E. Hendricks.[32] The non-phenol portion of this oil was found to consist of 10 per cent of an alcohol, while the greater part of the remainder is cymene and dextrogyrate limonene.

THE MONARDA OILS

General Statement. Although, as has been previously stated, the first chemical observation of the Monarda species seems to have been Elsner's note on the pigment of *M. coccinea, (M. didyma L.)*, the oils first attracted the more general attention of chemists. Nor is this in the least surprising, since the not unpleasant aromatic odor of the several species readily indicated the presence of volatile oils. Moreover, the spontaneous separation of the crystalline stearoptene from at least one of the oils, when exposed to ordinary winter temperature, well nigh forced itself upon the chemist's notice. Indeed, according to Flueckiger, nearly forty years before Elsner made his observations, the Apothecary Brunn of Guistrow, in 1796, had noticed a crystalline deposit in the oil of *Monarda didyma* * *L.*, which plant had probably been introduced from America.

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[31] *Ph. Rev.*, 14, p. 223; also *Proc. Am. Ph.*, 44, p. 238.

[32] *Ph. Arch.*, 2, p. 73.

* In all probability *Monarda punctata*, not *didyma* as stated by Flueckiger. Semmler is of the opinion that the stearoptene observed by Brunn was paraffin now known to exist in the oil of *M. didyma* (Die aetherischen Oele, Bd. 1, p. 345).

As a matter of fact, the work progressed exactly as one would expect. In 1845, Procter reported on the crystalline product, called it monardin, compared it with camphor, and studied its physical properties. In the next year Arppe practically repeated Procter's work and in addition determined the elementary composition of the stearoptene, while in 1884 Flueckiger identified it as thymol.

The chemists of Schimmel & Co. also examined specimens of "monarda oil" and reported upon its thymol content at various times, but nothing further was known of its composition till the publication of Schroeter's work in 1888 attracted the attention of chemists in this laboratory. From the summer of 1894, when Professor Kremers first began working with the Monardas, until the present time, there has been scarcely a season when some one here has not been at work upon some species of this genus, and by far the greater portion of this work has been upon the oils, though these comprise not more than 1 per cent of the fresh herb, and in one instance much less. Inasmuch, however, as the separation of the volatile components of a plant can readily be effected from the non volatile ones, even on a large scale, this work followed the line of least resistance, at least in so far as the isolation of the materials for study was concerned.

OIL FROM MONARDA CITRIÒDORA

PERCENTAGE YIELD. The yield from 50 pounds of the dried flowering herb of *M. citriodora* distilled in this laboratory in 1903[1] was about 1 per cent.

PHYSICAL PROPERTIES. *Color.* The color of the oil was reddish, as was also that of the oils distilled in 1904[2] and 1907, the latter being the darker of the two.

Odor. As the name of the species would indicate, this oil has a lemon-like odor.

Specific gravity. The specific gravity of the oil obtained by Brandel was 0.9437 at 20°. The specific gravity of the oils obtained in 1904 and 1907 was determined in 1908 by La Febvre, that of the former being 0.9603, that of the latter 0.9548.

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[1] *Ph. Rev.*, 22, p. 153.

[2] Mid. Drug. Ph. Rev., 44, p. 526.

Angle of Rotation: Apparently not determined.

CHEMICAL CONSTITUENTS. *Hydrocarbons.* The presence of hydrocarbons in the oil from *M. citriodora* has not been definitely established. Tests for limonene and phellandrene gave no positive results. The test for cymene by oxidation to hydroxy cuminic acid gave a crystalline precipitate melting at 124°, whereas the hydroxy derivatives of cuminic acid melts at 156°. The amounts of material with which these tests were made were necessarily small.

Phenols. Monatomic. As stated above phenols are present in the oil to the extent of from 65 to 80 per cent. These were found by Brandel to consist of carvacrol with little or no thymol.

Diatomic. From the last portions of the distillate of the phenols, crystals of hydrothymoquinone (m. p. 140°) were separated.

Aldehydes. The amount of aldehyde in the 1903 oil, determined titrimetrically by Brandel by the normal sodium sulphite method was found to be 1.2 per cent; while the 1908 oil, as determined by Le Febvre, was found to contain about 4 per cent of aldehydes. The odor of the oil would seem to indicate that this aldehyde is, at least in part, citral, but sufficient amounts of material have not yet been studied to admit of chemical identification.

Quinones. The red color of the oil, together with the presence of hydrothymoquinone would indicate the presence of thymoquinone, part of which, at least, is combined with the hydrothymoquine to form thymoquinhydrone. However, thymoquinone, itself, has not yet been isolated from the oil.

OIL FROM MONARDA DIDYMA

PERCENTAGE YIELD. The yield of oil from ***Monarda didyma*** is very small. In 1903, Brandel[1] obtained a yield of but 0.03 per cent from the dry herb purchased from Peek & Velsor of New York. Schimmel & Co.[2] report a yield of 0.096 per cent of oil from nearly dry stalks and leaves, and 0.32 per cent from the half faded blossoms.

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[1] *Ph. Rev.*, 21, p. 109.

[2] Sch. & Co's *Report*, Nov., 1908.

That the yield from the blossoms should be so much greater than from the stalks and leaves seems somewhat surprising when comparison is made with *M. fistulosa,* where we find the greatest amount of oil in the leaves with only small amounts in the corollas. However, the report of Schimmel & Co. does not state whether only the corollas or the entire flower heads or even the flowering tops were distilled.

PHYSICAL PROPERTIES. *Color.* The oil distilled by Brandel was of a light reddish-brown color, that reported by Schimmel & Co. was pale yellow.

Odor. Brandel mentions a sweetish balm-like odor, free from the smoky odor characteristic of phenols. Schimmel & Company speak of a lavander-like odor and a faint odor of ambergris.[1]

Specific Gravity. The specific gravity of the oil seems to be low compared with that from other species of Monarda. Brandel records a density of 0.902 at 20°, while Schimmel & Co. give 0.8855 at 15° for the oil from the stalks and leaves and 0.8665 for that from the blossoms.

Angle of Rotation. Brandel's oil turned the plane of polarized light about 10° to the left. Schimmel & Co. give

$[\alpha]_D = -15^\circ\ 45'$ for the oil distilled from leaves and stalks, and
$[\alpha]_D = -7^\circ\ 30'$ for the one from the blossoms.

CHEMICAL CONSTITUENTS. As mentioned above no thorough chemical examination of the oil from *M. didyma* appears to have been made, hence our knowledge of its constituents is rather scanty.

Hydrocarbons: Paraffin. Schimmel and Company describe all the oils obtained by them as being soluble in 70 per cent alcohol with difficulty and rich in paraffin.

Phenols, Monatomic. The low specific gravity would indicate the absence of phenols in quantity. Brandel found that his oil gave no reaction whatever for either thymol or carvacrol with Flueckiger's test. It is no doubt due to the absence of phenol as well as to the small amount of oil present in this plant that this species was selected by the early settlers as a substitute for Chinese tea.

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[1] *Ber. S. & Co.,* Oct., 1909, p. 80.

Diatomic. The presence of dihydroxythymoquinone in an extract from the blossoms of *M. didyma* is indicated by the green precipitate with lead acetate. Its presence in the oil, however, still remains to be proven.

OIL OF MONARDA FISTULOSA

PERCENTAGE YIELD. It is almost impossible to make any accurate general statement concerning the yield of oil obtained from this species since there has been no uniformity in the manner of handling the herb to be distilled. Sometimes it has been dried before distilling, but more frequently it has been distilled "as fresh as possible," which probably means that the plant had been cut anywhere from two or three hours to as many days before the oil was extracted. We meet with a similar difficulty in attempting to state with any degree of accuracy the comparative amounts of oil to be obtained from different parts of the plant or at different stages of growth. From the data at hand one might estimate that the amount of oil contained in the fresh herb is considerably less than 1 per cent, probably between 0.5 per cent and 0.75 per cent. Systematic experiments are under way during the present season to ascertain the exact yield.

It has been found (Mead,[1] 1895) that the stems are almost devoid of volatile oil, and that only a small amount of oil is to be obtained from the corollas.[2] Inasmuch as the seeds do not appear to contain any oil, it is probably safe to conclude that the greater portion of the oil comes from the leaves.

PHYSICAL PROPERTIES. *Color.* The oils from *M. fistulosa*[3] vary in color from almost colorless, i. e. pale straw color, to a deep red-brown when distilled; often, also, an oil that is nearly colorless when fresh turns to a red or even brown color upon standing.[4] It has been noticed that the dark colored oils[5] and those that acquire the dark color upon standing are obtained by distilling material including either the stem or flowers, or both. An oil obtained from the corollas alone[6] was of a very dark reddish-brown color, while an oil distilled from the leaves alone[6] was of a pale straw color and did not darken upon standing. Even today, after more than eight years, it still retains its straw-yellow color.

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[1] *Ph. Rev.*, 13, p. 207.

[2] *Ph. Rev.*, 21, p. 111.

[3] *Ph. Rund.*, 13, p. 207; also *Ph. Rev.*, 14, p. 198.

[4] *Ph. Rev.*, 19, p. 202.

[5] *Ph. Rev.*, 21, p. 111.

Specific Gravity. But little can be gained from a study of the physical constants of this oil. The specific gravity of the oils studied varies from 0.916, that of an oil distilled from stems and leaves[7] to 0.9589, that of an oil distilled from the corollas.[8] Moreover, there seems to be no regularity in the variation. Although, the highest specific gravity has been found to be that of an oil from the corollas alone and the most dense oils have always been obtained from herbs in bloom, and though the oils of the least density have been obtained from leaves and stems, or leaves alone, yet some oils from leaves and stems or from leaves alone have been as dense as some of those obtained from the entire herb, including blossoms. There has been also a great variation in the density of oils obtained in different years. During some years all of the oils have been light and during others heavy. The average specific gravity for all oils from *M. fistulosa* is about 0.9355.

Angle of Rotation. There is no more uniformity in the angle of rotation than in the specific gravity. In the majority of cases $[a]_D$ = about -1.4° though as high as -1.8° and as low as -0.15° have been recorded. Nor does the specific rotation seem to bear any definite relation to the part of the plant distilled.

CHEMICAL CONSTITUENTS. *Separation of the Components.* The accepted method of studying the oils has been to dissolve out the phenols by shaking with a dilute solution of caustic alkali, then, after separating the aqueous solution from the remaining oil, to regenerate them by the addition of an acid and to purify them by subsequent distillation with steam. In this way the percentage of phenols, by volume, was ascertained at regular intervals for two consecutive seasons, twelve samples being tested each year.[9] It varied but little and averaged 67.025 per cent. The percentage of phenols by forming the diphenol diiodide and titrating the excess of iodine with N/10 sodium thiosulphate, was found to be 55.93 per cent as an average of twelve samples.[10] (Alden.)

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[6] *Ph. Rev.*, 21, p. 113.

[7] *Ph. Rev.*, 21, p. 111.

[8] *Ph. Rev.*, 14, p. 100.

[9] *Ph. Rev.*, 15, p. 87.

For a more detailed examination, the non-phenol portion of the oil was fractionated into fractions covering about two degrees of temperature each,[11] from below 165° to 240°+.

Hydrocarbons: Limonene. In 1899 Brandel[12] by the formation of limonene nitrol benzylamine (m. p. 93°) identified limonene in the oil distilled in that year.

Cymene. The presence of cymene in a fraction of the oil, distilled in 1895, was established by Mead and Brennan[13] by its oxidation to hydroxy cumic acid (m. p. 156°).

Phenols. Monatomic. In 1895, in their first study of the oil from *M. fistulosa* Mead and Brennan[13] showed conclusively that the large amount of phenols in the oil, from 50 to 60 per cent, consists largely of carvacrol responding as it does to all tests for this phenol. That none, or less than two per cent, of the isomeric phenol, thymol, is present was demonstrated by Brandel,[14] in 1899, by the failure to obtain the brick-red color of dithymol diiodide when conducting experiments for the iodometric estimation of thymol and carvacrol.

Diatomic. In 1901, Brandel[15] separated from the phenol portion of an oil from *M. fistulosa* white crystals which melted at 140° and proved (Lieberman's quinhydrone reaction) to be the diatomic phenol hydrothymoquinone.

In the course of the first chemical study of the oil from *M. fistulosa* conducted in Professor Kremer's laboratory in 1895[16] some red crystals separated in the condenser while a small amount of phenols was being distilled. (Mead.) These crystals resembled alizarin in general appearance and behavior toward alkalies. They were not again obtained from the oil till 1907 when Suzuki,[17] while redistilling the phenol portion of an oil that had become decidedly red upon standing, found the red crystals separating in the condenser as before. By a series of parallel experiments with the red crystals and alizarin, Suzuki proved that they could no longer be referred to as "alizarin-like," but failed to establish their identity. In 1909, the writer[18] identified these crystals as dihydroxythymoquinone and showed that, by shaking with caustic alkali, thymoquinone can be oxidized so that upon distilling with water vapor the red crystals will separate in the condenser. In the fall of 1909, by means of the characteristic green precipitate with lead acetate, the presence of this diatomic phenol diketone was indicated in extracts from both the highly colored autumn leaves and the purple stems. Hence its occurrence in the oil may be assumed.

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[10] *Ph. Rev.*, 15, p. 87.
[11] *Ph. Arch.*, 2, p. 76.
[12] *Ph. Arch.*, 2, p. 77.
[13] *Ph. Rund.*, 13, p. 207.
[14] *Ph. Arch.*, 2, p. 78.
[15] *Ph. Rev.*, 19, p. 244.
[16] *Ph. Rund.*, 13, p. 207.

Quinones. While Brandel[19] in 1901 was purifying, by distilling with water vapor, the oil obtained from *M. fistulosa* during the seasons of 1899 and 1900, yellow crystals separated in the condenser toward the close of the process. These crystals were collected and identified with thymoquinone by means of elementary analysis, melting point, and preparation of the hydrochloride. The occurrence of thymoquinone in this oil, together with hydrothymoquinone, which was separated from the phenol portion of the same oil, was of great significance, since it suggested an explanation of the production of dark colored oils, either in the plant or upon standing, as well as the occurrence of the purple pigment found in stem and flowers.

Alcohol. With the mention of an alcohol, possibly $C_{10}H_{17}OH$[20] which is apparently present in the oil, the list of known constituents of *M. fistulosa* is complete. The presence of an alcohol in the non-phenol constituents of the oil was ascertained by Brennan and Mead[21] in 1895 but the identity of the alcohol has not yet been established. The possible presence of citral in *M. citriodora* might be taken as an indication pointing toward linalool or geraniol.

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[17] Mid. Drug. Ph. Rev., 44, p. 342.
[18] *Proc. A. Ph. A.*, for 1910.
[19] *Ph. Rev.*, 19, p. 200.
[20] *Ph. Rev.*, 19, p. 200.
[21] *Ph. Rund.*, 13, p. 211.

OIL FROM MONARDA PUNCTATA

PERCENTAGE YIELD. From the work that has been done upon the oil of *M. punctata*[1] it appears that the yield of oil from plants collected while in blossom, the early part of August, and distilled while fresh, corresponds to about 1 per cent of the fresh herb, while young plants[2] not yet in blossom, collected May 31, yielded 3.39 per cent of the partly dried herb. No effort seems to have been made to ascertain from what part of the plant the greater portion of the oil is obtained.

PHYSICAL PROPERTIES. *Color.* The oil mentioned above as distilled from the flowering plants was pale yellow, or light amber in color. That from the young plants of a slightly reddish color. The oil from plants collected Aug. 7, and distilled on Sept. 4, '09, became of a deep red color upon standing for four months, though it was of a yellow color when freshly distilled.

Specific Gravity. The specific gravity of the oils from the flowering plant has been 0.93+ in every instance. From the young plants it was 0.925, at 20°.

Angle of Rotation. The oil is almost optically inactive. In one instance $[a]_D = +0.0588°$ was observed.

CHEMICAL CONSTITUENTS. *Separation of the Components.* In studying this oil the phenol portion has been separated from the non-phenol portion and the non-phenol portion fractionated, as in the study of *M. fistulosa* recorded above. The oil has thus been found to contain from 56 to 62 per cent of phenols. Upon the removal of the phenols the specific gravity of the remaining oil was lowered to from 0.85 to 0.88 while the oil became somewhat stronger dextrorotary.

Hydrocarbons. Limonene. In 1899 Hendricks[3] by the formation of limonene nitrol benzylamine established the presence of a small amount of limonene in fraction 170° to 180°.

Cymene. By the formation of hydroxycumic acid from the fraction 170° to 178° of the non-phenol portion of an oil, Schumann[4] in 1896 identified cymene.

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[1] *Ph. Rev.*, 14, p. 223; Proc. *A. Ph. A.*, 44, p. 238. *Ph. Arch.*, 2, p. 73.

[2] *Ph. Rev.*, 14, p. 223; Proc. *A. Ph. A.*, 44, p. 238.

[3] *Ph. Arch.*, 2, p. 73.

[4] *Ph. Rev.*, 14, p. 223.

Phenols. Monatomic, Thymol. As stated before, Procter[5] in 1845 reported upon the crystalline product from the oil of *M. punctata*, which Flueckiger[6] in 1884 identified as thymol. This phenol has been found to be present to the extent of about 60 per cent of the entire oil.

Carvacrol.[7] It is believed that sometimes at least carvacrol is present in the oil of *M. punctata* with its isomer.

Diatomic. The presence of the diatomic phenol hydrothymoquinone in the oil of *M. punctata* has never been definitely established, though its presence, together with its oxidation product, thymoquinone, as quinhydrone would seem to be indicated by the purplish color of some of the stems, and by that of the bracts surrounding the flower heads.

Alcohol. By acetylization of the non-phenol portion of the oil, Hendricks demonstrated the presence of an alcohol, the identity of which has not been established, to the extent of about 10 per cent of the non-phenol portion.

MONARDA PIGMENTS

In the review on the chemical work of the Monardas, it has already been pointed out that the earliest published chemical work on the Monardas pertains to the red pigment found in the corollas of *Monarda didyma.* Indeed, the inflorescences of this species are so attractive that the plant is cultivated, especially for border purposes. The inflorescences of at least two other species, which have been examined thus far, viz.: those of *M. punctata* and *M. fistulosa* are likewise very attractive. The corollas of the former are greenish-yellow with dark brown dots, those of the latter are of a delicate purple. By proper combination of these three species it ought to be possible to bring about very handsome color effects in park borders.

Although to the eye there is a great difference in the color effects of the species enumerated, the chemical investigations of the pigments indicate a very close chemical relationship. This relationship holds true not only for the colored substances producing the pigmentation of the plant, but for the volatile substances found in the volatile oils as well. Indeed, the arbitrary distinction drawn by the chemist between pigment and volatile oil is not at all maintained by the plant itself.

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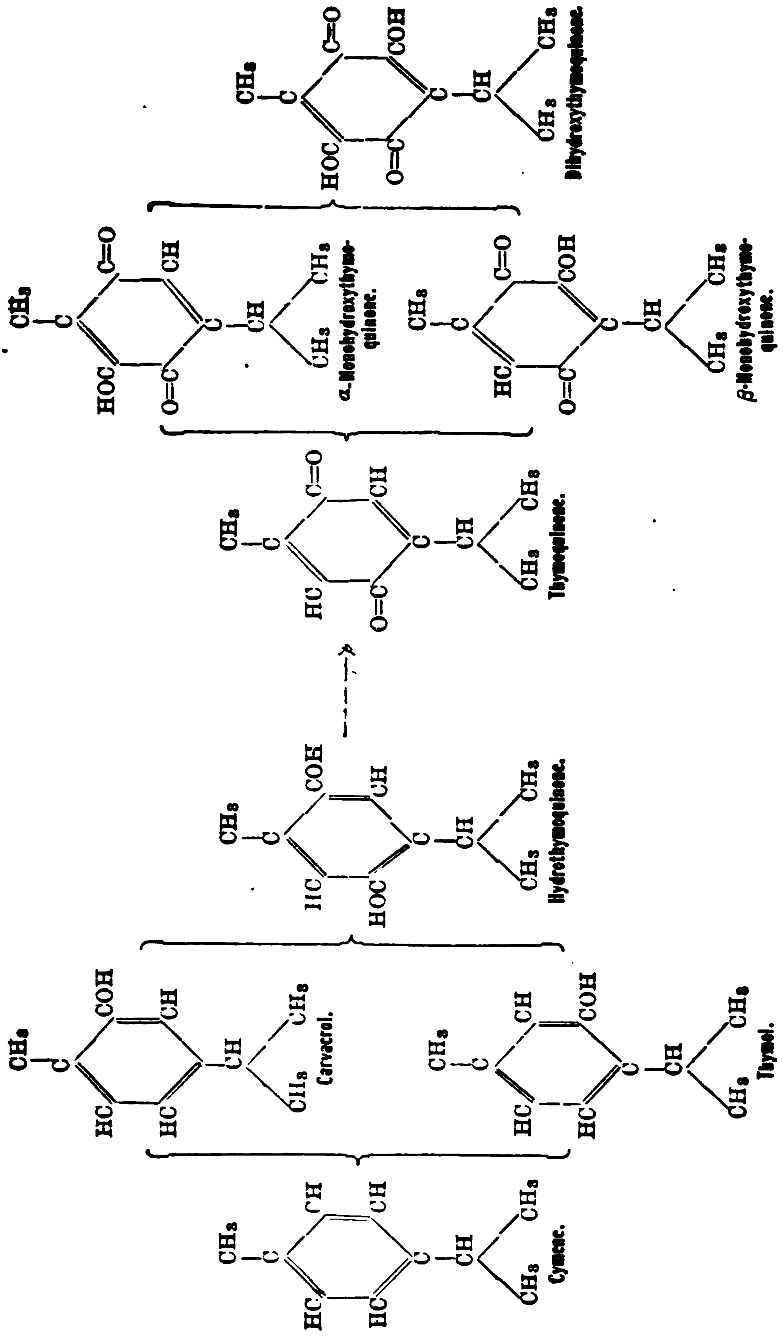
[5] *Am. J. Ph.*, 17, p. 86.
[6] *S. & Co. Ber.*, Sept., '84, p. 12.
[7] *Ph. Arch.*, 2, p. 76.

Attention has already been directed to Belhomme's (1856) supposition that the red pigment from *Monarda didyma* might be identical with the red pigment of cochineal; also to the fact that the red crystalline pigment isolated from *Monarda fistulosa* by Mead (1895) was for a time referred to as alizarin-like, in order to distinguish it from the crystalline thmyoquinhydrone pigment isolated (1903) from the flowers of *M. fistulosa.* Finally, it has also been pointed out that this "alizarin-like" pigment has been identified by the writer as dihydroxythymoquinone. That small amounts of a mixture of dihydroxythymoquinone with its quinhydrone should be pronounced as "alizarin-like" is readily understood if it be remembered that both substances are diketones as well as diphenols, hence give the same type reactions.

The relation of the pigment substances to each other and to the volatile constituents of the Monardas, also the role which some of the non-colored volatile and non-volatile substances play in the formation of the pigments, can best be illustrated by a series of graphical formulas given on the accompanying chart.

From the following chart it becomes apparent that here we have to deal with white (or colorless), yellow, orange, and red substances, all of which are very closely related to each other. Moreover, the thymoquinone, monohydroxythymoquinone and dihydroxythymoquinone, have the capacity of adding monatomic phenols, thus yielding highly colored phenoquinones; also diatomic phenols thus yielding the equally highly colored quinhydrones. The isolation of the thymoquinhydrones from the corollas of *Monarda fistulosa* has already been mentioned. Likewise has the formation of phenoquinones and quinhydrones of mono- and dihydroxythymoquinone been referred to as a probable explanation of the complexity of the mixture of crystalline pigment originally referred to as "alizarin-like." The following table


Cymene.
Carvacrol.
Thymol.
Hydrothymoquinone.
Thymoquinone.
α-Monohydroxythymoquinone.
β-Monohydroxythymoquinone.
Dihydroxythymoquinone.

illustrates the phenoquinone and quinhydrone pigments that can result from the addition of the phenols to the quinones thus far observed in the Monardas.

Quinones	*Phenoquinones*	*Quinhydrones*
Thymoquinone	1.) With two molecules of thymol. 2.) With two molecules of carvacrol. 3.) With one molecule each of thymol & carvacrol. 4.) With two molecules of α-monohydroxythymoquinone. 5.) With two molecules of β-monohydroxythymoquinone. 6.) With one molecule each of α- & β-monohydroxythymoquinone. 7.) With one molecule each of α-monohydroxythymoquinone and thymol. 8.) With one molecule each of α-monohydroxythymoquinone and carvacrol. 9.) With one molecule each of β-monohydroxythymoquinone and thymol. 10.) With one molecule each of β-monohydroxythymoquinone and carvacrol.	1.) With hydrothymoquinone. 2.) With dihydroxythymoquinone.
α-Hydroxythymoquinone.	1.) With two molecules of thymol. 2.) With two molecules of carvacrol. 3.) With one molecule each of thymol and carvacrol.	1.) With hydrothymoquinone. 2.) With dihydroxythymoquinone.

Quinones	*Phenoquinones*	*Quinhydrones*
	4.) With two molecules of α-monohydroxythymoquinone.	
	5.) With two molecules of β-monohydroxythymoquinone.	
	6.) With one molecule each of α- and β-monohydroxythymoquinone.	
	7.) With one molecule each of α-monohydroxythymoquinone and thymol.	
	8.) With one molecule each of β-monohydroxythymoquinone and carvacrol.	
	9.) With one molecule each of β-monohydroxythymoquinone and thymol.	
	10.) With one molecule each of β-monohydroxythymoquinone and carvacrol.	
β-Hydroxythymoquinone.	1.) With two molecules of thymol.	1.) With hydrothymoquinone.
	2.) With two molecules of carvacrol.	2.) With dihydroxythymoquinone.
	3.) With one molecule each of thymol and carvacrol.	
	4.) With two molecules of α-monohydroxythymoquinone.	
	5.) With two molecules of β-monohydroxythymoquinone.	
	6.) With one molecule each of α- and β-monohydroxythymoquinone.	

Quinones	*Phenoquinones*	*Quinhydrones*
	7.) With one molecule each of α-monohydroxythymoquinone and thymol. 8.) With one molecule each of α-monohydroxythymoquinone and carvacrol. 9.) With one molecule each of β-monohydroxythymoquinone and thymol. 10.) With one molecule each of β-monohydroxythymoquinone and carvacrol.	
Dihydroxythymoquinone.	1.) With two molecules of thymol. 2.) With two molecules of carvacrol. 3.) With one molecule each of thymol and carvacrol. 4.) With two molecules of α-monohydroxythymoquinone. 5.) With two molecules of β-monohydroxythymoquinone. 6.) With one molecule each of α- and β-monohydroxythymoquinone. 7.) One molecule each of α-monohydroxythymoquinone and thymol. 8.) With one molecule each of β-monohydroxythymoquinone and thymol. 9.) With one molecule each of α-monohydroxythymoquinone and carvacrol.	1.) With hydrothymoquinone. 2.) With dihydroxythymoquinone.

10.) With one molecule each of β-monohydroxythymoquinone and carvacrol.

Taking into consideration only those compounds that have been isolated, (hydrothymoquinone, thymoquinone, and dihydroxythymoquinone) or whose presence has been indicated (monohydroxythymoquinone) in the Monardas thus far, the number of possible pigments becomes truly bewildering. A consideration of these possibilities of easily decomposable phenoquinones and quinhydrones readily explains why a crystalline pigment, seemingly a chemical unit, upon recrystallization from such a solvent as ether yields several kinds of crystals of different shades of red and purple. To attempt the isolation of a number of these pigments would be a thankless task. Indeed, after they had been isolated the question might pertinently be asked whether the combination as isolated existed as such in the plant or whether it had been formed because of a change of solvents. The practical task of the plant chemist, therefore, must be regarded as having been solved when he has isolated the components and has recognized the possibilities of combination. He will then be able to interpret numerous phenomena in his investigations which otherwise remain inexplicable.

However, the subject of the pigmentation of the Monardas is not solved even after the numerous combinations of phenoquinones and quinhydrones have been worked out. Not a few of these pigments are phenolic in character and hence can combine with metallic constituents of the plants giving rise to different shades of the original pigment. For a better understanding of these, reference must be had to the inorganic constituents of the Monardas.

MONARDA CITRIODORA. Owing to the difficulty in securing material, but little work has been done on pigmentation in this species. Hydrothymoquinone has, however, been isolated from the oil. The dark color of the oil when distilled would lead one to suppose that part of the hydrothymoquinone is oxidized in the plant to form thymoquinone which unites with the hydrothymoquinone to form the intensely colored quinhydrone, thus giving color to the oil. The response of the deep red phenol portion of the oil to the lead acetate test for monohydroxythymoquinone complicates matters somewhat, inasmuch as this compound dissolves in phenols with a deep red color, probably a phenoquinone. We have also reason to believe that monohydroxythymoquinone forms a quinhydrone with hydrothymoquinone, since a mixture of molecular proportions of the two substances in ether, purified by distilling over sodium, does not give a purple color with decolorized fuchsine solution, while either substance alone responds to this test.

MONARDA DIDYMA. It would be difficult to conceive of a more interesting and attractive subject for the study of plant pigmentation than *Monarda didyma.* Here we find an abundance of color, not only in the flower, but in the upper foliage leaves and the bracts surrounding the flower heads. In the study of this plant, however, we meet with added difficulties for while like *Monarda citriodora* it is rare and difficult to obtain in quantity, the yield of oil is so extremely small that an almost unlimited quantity of material would be required to carry out an extended examination of the pigments carried over with the volatile constituents by the process of distillation.

The little that is known, therefore, of pigmentation here has resulted from a study of alcoholic extracts of the flowers. Elsner, we have seen, in 1832, found that the red precipitate obtained upon evaporating this extract in aqueous solution gave a green precipitate with normal lead acetate and a reddish-purple color with basic lead acetate. These the writer has shown are reactions for dihydroxy- and monohydroxythymoquinone respectively. Belhomme also, in 1856, obtained the purple color with lead acetate, indicating the presence of monohydroxythymoquinone, also the violet color with calcium salts and crimson-violet with barium salts which might mean the presence of either hydroxy compound. Belhomme, however, interpreted these reactions as indicating the presence of carmine, identical with that obtained from the cochineal insect. The writer has in the same way repeatedly obtained the green precipitate indicative of dihydroxythymoquinone, but never the test for the monohydroxy compound.

Meager as these results are, they point to the presence of one or both of the hydroxythymoquinones in the blossoms and show a relation between *Monarda didyma* and the other species studied.

MONARDA FISTULOSA. Of all the Monardas thus far investigated *M. fistulosa* has proved the most satisfactory for the study of pigmentation. Not only have thymoquinone and hydrothymoquinone been isolated in quantity but the thymoquinhydrone itself has been separated from the oil distilled from the corollas. In addition to these compounds which would seem sufficient to account for all the color phenomena observed in the plant, dihydroxythymoquinone has been isolated from the oils and residues: first by Mead in 1895; then by Suzuki in 1906-7; and recently by the writer from both a sample of carvacrol from *M. fistulosa,* and a residue from distilling a phenol portion of the oil. Monohydroxythymoquinone has also been indicated, by the lead acetate reaction, in the residues as well as in the phenol oil.

Since dihydroxythymoquinone can, and probably does form a quinhydrone with hydrothymoquinone and since it undoubtedly forms a phenoquinone with carvacrol, we have here a more complicated case than that found in the oil from *M. citriodora* where we have, so far as we have any knowledge, only the monohydroxythymoquinone with which to deal. Evidence that dihydroxythymoquinone does form these complex compounds is furnished by traces of a purple quinhydrone that has been obtained upon evaporating a mixture of equimolecular proportions of dihydroxythymoquinone and hydrothymoquinone in ethereal solution. Such a mixture also gives no response to the fuchsine test, while either compound alone does. That it forms a compound with carvacrol from which dihydroxythymoquinone was crystallizing, is shown by the fact that the carvacrol in question gave, after filtering out the red crystals, no test with lead acetate, though the carvacrol was of a clear, deep red color. The formation of such a compound probably also accounts for the fact that no tests for dihydroxythymoquinone have ever been obtained in any Monarda oil, though red oils have been tested repeatedly.

That these highly colored substances are the direct product of the plant and are not necessarily formed in the oils upon standing is shown by the response to tests for dihydroxythymoquinone in the alcoholic extracts of the purple stems and red autumn leaves of *M. fistulosa*. The pigment in these highly colored parts, as well as in the blossoms, is probably present in the form of a quinhydrone, or a mixture of quinhydrones, of which dihydroxythymoquinone forms a part. The fact that this extract gives a colorless solution in alcohol which upon evaporation yields a highly colored residue lends weight to this supposition, since this is the characteristic behavior of quinhydrones. The reactions in alcoholic solution are peculiar and not fully understood, acids turning it red (presumably the free pigment), and alkalies green. The aqueous solution of the precipitate from the purple stem and colored leaves, however, gives a strong test for dihydroxythymoquinone with lead acetate.

MONARDA PUNCTATA. Meager as is our knowledge of the pigments in *M. citriodora* and *M. didyma*, it is much more meager in regard to those of *M. punctata*. And here it can not be attributed, as in the other instances to a scarcity of material with which to work. All of the chemical knowledge we possess of the pigments in this species is the response to tests for monohydroxythymoquinone in a small portion of the phenol oil, probably carvacrol, that did not solidify upon chilling to 0°. That quinhydrones are probably present in the plant is indicated by the purple color of some of the stems and the bracts surrounding the flowers, though no trace of thymoquinone or hydrothymoquinone has ever been found in any oil or extract from the plant. We are, moreover, wholly at a loss as to what to ascribe the yellow color of the corolla unless it be to thymoquinone.

FERMENTS

The chemistry of the volatile oils as well as that of the pigments shows that a group of closely related compounds is involved, all of which are oxidation products of cymene which also has been found in this genus. The biochemical study of this genus naturally necessitated the seeking of an answer to the question: Which of these cyclic substances is first formed from simpler chain compounds and which result subsequently as oxidation products. This oxidation may be assumed to be brought about by the direct addition of oxygen without intervention. Secondly, it may be brought about by the intervention of oxygen carriers, commonly designated oxidases. Thirdly, it may be due to autoxidation.

That autoxidation is by no means excluded becomes apparent from the behavior of hydrothymoquinone in different solvents, a study, the results of which have not yet been recorded. In this connection the peculiar behavior of alkalies and alkali earths should be mentioned. That direct oxidation without the intervention of an oxygen conveyor is also possible seems to be indicated by the behavior of carvacrol solutions of some of the substances found in the Monardas. Only observations, but no direct experiments have been made along this line.

As to the intervention of oxygen conveyors several possibilities should be indicated. That terpenes occur in the Monardas has already been pointed out. That at least several of the terpenes absorb oxygen, presumably forming peroxides, and that these supposed peroxides have the capacity to give off a part of the oxygen absorbed has been demonstrated in this laboratory.[1] As yet no experiments have been made to ascertain whether the terpene or terpenes found in Monarda belong to this class.

The second possibility lies in the presence of the so called oxidizing ferments or oxidases. That one of these has the capacity of oxidizing hydrothymoquinone to thymoquinone through the intervening thymoquinhydrone has been demonstrated innumerable times. Indeed, this reaction is so striking in character that it constitutes the most valuable oxidase test yet devised for laboratory experiment in biochemistry.

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[1] *Unpublished results* of H. F. Bandt.

That the Monardas also contain a ferment which appears to be able to oxidise thymol will be indicated in the results hereinafter recorded. Inasmuch, however, as it has been shown by the writer that in all probability Bourquelot's tyrosinase oxidizes thymol to dithymol, this particular oxidase does not help us to a better understanding of the oxidation of thymol or carvacrol to hydrothymoquinone by the plant. Indeed, as already pointed out, it is not at all impossible that the monatomic phenols are reduction products, possibly by-products of autoxidation. The large amounts, however, in which these two monatomic phenols are found in comparison to thymoquinone, does not speak for the probability of this possibility. Finally, although not commonly looked upon as oxygen conveyors, the influence of the metallic hydroxides on the oxidation products should not be lost sight of. Further reference to these possibilities will be made under inorganic constituents.

MONARDA FISTULOSA. In 1904 Rabak[2] demonstrated the presence of an oxidase in the leaves of *M. fistulosa* and its ability to oxidise hydrothymoquinone to thymoquinone with the formation of the pigment thymoquinhydrone as an intermediate product, thereby explaining the presence of this pigment in the plant and in the oil obtained from it. He also tried the action of the ferment upon the monatomic phenols, thymol and carvacrol, found so abundantly in the monarda species, as well as upon cymene, the hydrocarbon underlying all of these phenols, but with negative results.

During the same summer Swingle[3] ascertained the "thermal death point" of the ferment, finding that when heated for half an hour to 77° there was no longer a reaction with tincture of guaiac and only a few bubbles of oxygen evolved from hydrogen peroxide. When heated for the same length of time to 81° there was no longer action with either reagent.

In order to ascertain the relative amounts of oxidase which has the power to liberate oxygen from hydrogen peroxide in different parts of the plant and under varying conditions of growth, the writer[4] carried out a series of quantitative experiments during the summer of 1907 in which it was ascertained that the leaves which were greenest and gave the best evidence of vigorous growth contained the largest amount of oxidase. The amount found in leaves low down on the stem was never equal to more than one-half of that obtained from an equal weight of leaves from the growing tip. This is in accordance with the general notions held as to the vigor of a plant organ and its relation to ferment content.

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[2] *Ph. Rev.*, 22, p. 190.

[3] *Ph. Rev.*, 22, p. 193.

Leaves which had prematurely been colored red, as in the autumn were tested and found to yield but small amounts of oxidase, while the colored florets were found to contain only about one-tenth the amount of oxidase found in the vigorously growing leaves. A short series of experiments performed during the summer of 1909 confirmed these results. Fresh vigorous leaves at the top of the plant liberated about 100 cc of oxygen from hydrogen peroxide for each 0.5 gram of leaves used, healthy full grown leaves from the base of the plant about 40 cc of oxygen, and the colored florets only about 9 cc.

The presence of an oxidase by means of which the plant can oxidize hydrothymoquinone to thymoquine thus being established, the question which naturally presents itself next is this, can the plant aided by an oxidase pass from thymol or carvacrol to hydrothymoquine?

As becomes apparent from the series of oxidation products of cymene found in the Monardas, it is a matter of importance to ascertain which of these cyclic molecules is the first to be produced by the plant. A partial answer to this query may possibly be had by ascertaining which of these substances can be oxidized by the oxidase or oxidases of the plants in question. It should always be borne in mind that some of the lesser oxidized substances may result as reduction products in the process of autoxidation, or as dehydration products.

As already stated, Rabak obtained negative results by acting on the monatomic phenols with the Monarda oxidase. Bourquolot[5] in 1896 showed the presence of a ferment, tyrosinase, in *Russula delica,* which oxidises thymol and carvacrol, giving a white precipitate. Bourquolot's observations were verified by the writer and the white precipitate, examined microscopically, was found to correspond with dithymol obtained by oxidising thymol with ferric chloride. The action of tyrosinase is destroyed by the presence of 50 per cent alcohol, and Rabak had prepared his oxidase by precipitating with strong alcohol. Preparations were, therefore, made from monarda leaves without the use of alcohol. With tyrosine no red color was obtained and upon evaporation only a fine line of black around what had been the surface of the liquid. An aqueous solution of thymol was prepared and to 20 cc of this solution, in separate flasks, was added 5 cc of the aqueous extract of monarda, both alone and in the presence of various reagents, viz.: hydrogen peroxide, potassium hydroxide, sodium hydroxide, calcium hydroxide, potassium acid carbonate, and sodium acid carbonate. With the thymol alone as well as with calcium hydroxide the solution lost the brownish tinge due to the aqueous extract of the monarda; with the others no change was noted.

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[4] *Ph. Rev.*, 26, p. 314.

A large amount, 100 cc of thymol solution and 10 cc of monarda extract, was then allowed to stand for about two months. The solution became almost milky in appearance and a heavy brownish precipitate separated out. Under the microscope this appeared full of oil globules and granular like masses.

A monarda extract was prepared, using equal parts of glycerin and water as a solvent, and filtered till it remained perfectly clear, though brown in color. Two tests were carried out at the same time using 100 cc of the thymol solution to 5 cc of the monarda extract. One flask was set in a water bath and heated to 100° for about a minute while the other was not heated. The solution that had not been heated slowly became cloudy and a very perceptible brownish percipitate was formed, while the solution that had been heated remained perfectly clear for weeks. Though these tests are far from satisfactory, they are by no means negative, and they indicate that there is present in the extract from *Monarda fistulosa* something that acts upon thymol solution and that this action is apparently prevented, by heating the extract above the thermal death point of the ferment.

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[5] *C. r.*, 123, p. 423.

The glycerin extract seemed to have undergone no change during this period and still retained its activity toward guiac tincture.

MONDARA DIDYMA. Oxidase, soluble and insoluble, was prepared according to Rabak and subjected to the same tests previously recorded in connection with *M. fistulosa,* with the same results, except that with hydrothymoquinone the action was much slower. Quantitative determinations of oxidase were made, as with *M. fistulosa.* The results were similar, only about three-fourths as much oxygen being evolved with the same amount of material.

It was noticed in this series of experiments, as in those with *M. fistulosa,* that the most lively evolution of oxygen was produced by the young leaves at the top of the plants. These experiments by the writer were performed in the late fall and early winter of 1908, the hydrothymoquinone tests being made with young plants from the greenhouse.

MONARDA PUNCTATA. In the fall of 1908 oxidase was prepared from the leaves of *M. punctata,* as from *M. fistulosa* and *M. didyma* above, and the same tests made with similar results. In the summer of 1909, two quantitative tests of the amount of oxidase in the florets of *M. punctata* were made, and only about 3 cc of oxygen were liberated from hydroygen peroxide by 0.5 grams of the florets.

MONARDA RUSSELIANA. At the same time that the quantitative tests for oxidase in the blossoms of *M. punctata* were made, similar tests were made with the florets of *M. russullana* with similar results—only 2 or 3 cc of oxygen being evolved by 0.5 gram of the blossoms.

INORGANIC CONSTITUENTS

Aside from the general physiological significance which the inorganic constituents assume in the function of the osmotic pressure of the sap, these mineral substances, no doubt, perform a variety of specific functions. Of but a few of these have we any proper conception. The most conspicuous which the chemical study of the monardas has thus far revealed is the role which the metallic elements apparently play in the pigmentation of the various parts of the plant.

Whatever the pigment thus far isolated, be it an hydroxythymoquinone or a quinhydrone, all appear to be phenols in character containing hydrogen atoms readily replaced by metallic elements or positive groups. These basic derivatives of the organic pigments differ more or less in color and are apparently responsible for some of the different shades of the same fundamental pigment. In connection with the quinhydrones a special study has been made of this aspect of the pigmentation of the monardas. However, nothing very definite is as yet known as to the particular kind of metallic derivative that may be found in e. g. the floral leaves of the several species.

A mere beginning has thus far been made by ascertaining the ash content of the different parts of *Monarda fistulosa.* Thus 10.21 p. c. of ash have been obtained from the leaves;[1] 3.22 p. c. from the stems.[2] In addition the floral leaves of *Monarda fistulosa* used in the distillation of the oil were dried and later incinerated. Thus a comparatively large amount of ash was obtained and partly analyzed. The results of this work, however, have been lost, as other valuable material was lost in the course of moving the laboratory in 1904. Only a few borax beads indicating the presence of cobalt in the ash remain to tell but an insignificant part of the story. As soon as more floral material becomes available this work ought to be repeated not only for *Monarda fistulosa* but for all species of Monarda.

The acid radicles may also influence, though indirectly, the pigmentation of the plant. Thus e. g. phosphates in solution, in all probability slightly acid phosphates, may react with the metallic element of a bluish pigment molecule, resulting in the crystallization or other deposition of a neutral phosphate molecule and the freeing of the organic pigment molecule from its inorganic components. The change of blue floral leaves to red with the deposition of submicroscopic crystals has been observed several times but not in connection with Monarda material.

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[1] Average of five determinations.

[2] Average of three determinations.

A possible influence of basic inorganic material remains to be referred to, viz.: the stimulating influence some of them, such as potassium hydroxide and calcium hydroxide, exert on oxidizing reactions, e. g. the oxidation of thymoquinone. That even very dilute basic solutions exert such an influence has been shown by the action of lime water upon aqueous thymoquinhydrone solution. It has further been demonstrated by Schaer[1] and others that traces of basic substances stimulate the action of oxidases.

So far our knowledge of the inorganic constituents of the Monardas is altogether too limited to suggest even probabilities. Only surmises can be expressed.

WATER

Although but little of importance may be expected from the determination of the water content of the different parts of the plants studied, it seems desirable, nevertheless, to make such determinations. Thus e. g. it ought to prove of some interest to determine the ratio between water content and oxidase in young leaves and old leaves. The water content of the several parts of *Monarda fistulosa* is possibly not without significance. Thus material collected in the fall of 1904 yielded the following results:—

Roots	Stems	Leaves	Flower tops
55.6 p. c.[2]	55,76 p. c.[3]	71.75 p. c.[4]	27.91 p. c.[5]

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[1] From a reprint from the *Pharm. Inst. Strassburg,* 1902.

[2] Average of eight determinations.

[3] Average of nine determinations.

[4] Average of eight determinations.

[5] Average of five determinations.

It would seem but rational to assume that the chemical activity in the floral leaves is fully as great as that of the green foliage leaves, yet the aqueous medium in which these reactions mostly take place is much smaller in quantity in the former than in the latter. A more careful study e. g. of the saccharine, volatile, and pigment materials of both organs may bring out striking analogies between the respective chemical changes and water content. Thus far only a partial comparison can be made between the volatile oils of floral and foliage leaves. The former is rich in quinhydrone, whereas the latter contains quinhydrone only when the leaves have been allowed to wilt for some time, i. e. when the oxidase of the leaves has had time to produce the necessary components, the thymoquinone. This study should also be extended so as to yield a larger variety of observations on material collected at different times during the summer.

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Elsner, L. 1832

Ueber den rothen Farbestoff in den Blumenblaettern und einigen andern Pflanzentheilen.

Chem. Centralbl., 3, p. 571.

The dried pigment of *M. Coccinea* is a beautiful purple red, gives, in aqueous solution, a bluish-green precipitate with basic lead acetate and a violet-red precipitate with lead acetate.

Procter, Wm., Jr. 1845

Observations on monardin, a peculiar crystalline substance, derived from the volatile oil of Monarda punctata.

Am. J. Ph., 17, p. 86.

The author reports the occurrence of a crystalline product in the volatile oil of horsemint. He compares its appearance to that of camphor, and calls it monardin. It melts at 118°F (48°C) and boils at 413–418°F (211.5°C). This was evidently thymol, not known to occur in horsemint oil at that time.

Arppe, A. E. 1846

Notiz ueber das Monardaoel.

Annalen, 58, p. 41.

The earliest authentic work on *Monarda punctata* oil was done by Arppe in 1846. His principal work was on the solid stearopten of the oil. It melted at 48° and boiled at 220°. On analysis he obtained C = 80%, H = 9.52%, O = 210.48%. He evidently did not recognize it as a phenol, especially not as thymol, his work being almost entirely on physical properties and constants of the stearopten.

Belhomme. 1856

Matiere tinctoriale extraite de la Monarde ecarlate.

Compt. Rend., 43, p. 382.

The "Monarde ecarlate," *Monarda didyma L,* is stated to contain carmine, a substance that has previously been found only in the fruit of the cactus and in the cochineal insect. The color is located in the corollas and is soluble in water.

Calcium carbonate colors it violet, lead acetate violet, HCl or H_2SO_4 red-orange, KOH yellow, ammonia red-brown, $Ba(OH)_2$ crimson-violet, $(NH)_2SO_4$ decolorizes. These reactions are like those of carmine. When boiled with alcohol it deposits a precipitate of carmine upon cooling. The pigment may be used to color silk and the author thinks it would prove of importance to the silk industry.

Flueckiger, F. A. 1878

Nachschrift von Prof. Flueckiger.

Arch. d. Pharm., 212, p. 488.

In 1796 the apothecary Brunn of Guestrow observed a crystalline deposit in the oil of *Monarda didyma* L., which apparently was introduced from America at that time.

Schimmel & Co. 1884

Oil from Monarda punctata L.

Ber. S. & Co., Sept. 1884, p. 12.

The distillation of an oil from *Monarda punctata* was accomplished by S. & Co's New York branch. The presence of thymol was identified by Prof. Flueckiger.

Schimmel & Co. 1885

Oil from Monarda punctata L.

Ber. S. & Co., Sept. 1885, p. 20.

According to the chemists of S. & Co., horsemint oil contains from 20–30 per cent of thymol.

Schroeter, J. M. 1888

Am. Journ. Pharm., 60, p. 1. [Ber. S. & Co., Oct. 1888, p. 26.]

J. M. Schroeter examined what was supposed to be the volatile oil of *Monarda punctata*. One sample kept at the Philadelphia college of Pharmacy for a number of years, had a crystalline deposit of thymol. Samples II and III were commercial samples, but no thymol was deposited from them even on cooling to –15°C. On treating the fraction above 200°C with caustic soda and precipitating it with HCl, no crystalline product could be obtained. Thus, evidently, carvacrol was present instead of thymol. The most important constituents of the oil were found to be a hydrocarbon, $C_{10}H_{16}$, laevogyrate and present to the extent of about 50 per cent. Thymol $C_{10}H_{14}O$, dextrogyrate and present to the extent of about 25 per cent. Higher oxygenated compounds $C_{10}H_{18}O$. Also formic, acetic and butyric acids.

Kremers, E. 1895

On the chemical composition of the volatile oil from Monarda fistulosa (L).

Pharm. Rundschau, 13, p. 207.

The oil was obtained in this case from *Monarda fistulosa*, identified by Prof. L. S. Cheney. The phenol part of the oil was shown to be carvacrol. A number of the derivatives were prepared to compare them with the same derivatives obtained from thymol. A crystalline red coloring matter was obtained while distilling the phenol oil, which melted at 219–223°. The behavior of this substance toward alkalies suggested a substance related to alizarin. The non-phenol oil was carefully fractionated and combustions made of fraction 167°, giving as a formula $C_{10}H_{14}$ or $C_{10}H_{16}$, likewise with fraction 173–174°. The residue 200°+ was saponified and fractionated. Fraction 225–235° indicated the composition $C_{10}H_{16}O$. The mixed fractions after oxydation with chromic acid, were tested for cymene, oxycumic acid melting at 156° being prepared.

Melzner, E. H. & Kremers, E. 1896

On the chemical composition of the oil from Monarda fistulosa (L).

Ph. Rev., 14, p. 198.

Monarda fistulosa herb was collected during a period of 12 weeks and each part distilled separately. The specific gravity, rotary power and percentage of phenol of each distillate was determined:

Sp. gr.	0.911 to 0.936.
Rotary power	1° 32′ to 3° 16′ in 200 mm.
Per cent phenol	58–72 per cent.

Non-phenol oil was fractionated in small fractions, quantity, specific gravity, and $[a]_D$ were determined.

Schumann, W. R. & Kremers, E. 1896

On the chemical composition of the oil from Monarda punctata (L).

Ph. Rev., 14, p. 223.

An examination of *Monarda punctata* collected at Pine Bluff. Phenol content was found to be 56 per cent. The non-phenol oil was fractionated into portions of about 10°. Cymene was identified in fraction 172–178° by converting it to oxycumic acid. Fraction 186–202° upon combustion yielded results corresponding to $C_{10}H_{18}O$. Young plants collected in May yielded 3.39 per cent of oil containing 61 per cent of thymol.

Melzner, E. J.

The phenol-content of the oil of Monarda fistulosa (L).

Pharm. Rev., 15, p. 86.

This is a continuation of the work published a year previous. The report consists of the results of the assay of the phenol content, 11 samples, of the oil of *M. fistulosa*. The oil was assayed both by shaking out with alkali and by titration with N/10 iodine solution. An average yield of 66.96 per cent of phenol was obtained with the alkali method and an assay of 55.64 per cent with the titration method.

Kremers, E. 1899

On the chemical composition of the monarda oils: Monarda fistulosa (L.)

Pharm. Archives, vol. 2, p. 16.

During the summers of 1895 and 1896 oil was distilled almost weekly. Fractions 174–176° and 176–178° oxidized without yielding hydroxycuminic acid. Acetic acid found in mother liquor. Oil distilled during summer of 1898 yielded 1 per cent of the fresh herb. Upon shaking with caustic soda 68 per cent of oil went into solution. Where phenol fractions were exposed to a freezing mixture of ice and salt it congealed but melted upon separating. Carvacrol congeals at -20° and melts at 0°. Phenol found to contain less than 2 per cent of thymol.

Hendricks, W. E. and Kremers, E. 1899

On the chemical composition of monarda oils: Monarda punctata (L.)

Pharm. Archives, 2, p. 73.

Oil distilled from plants collected near Arena, Wis. and identified by Prof. Cheney. Yield 1 per cent of oil, light color, pleasant odor, sp. gr. at 15° 0.932, almost inactive toward polarized light. Contained about 62 per cent phenol. Phenol removed by precipitation from alkaline solution with H_2SO_4 and exposure to cold, crystals recrystallized from glacial acetic acid m. p. 50.5°.

Non-phenol portion found to contain no ester and about 10 per cent of an alcohol, the larger portion being a fraction boiling 170–180°, consisting of cymene and dextrogyrate limonene.

Brandel, I. W. and Kremers, E. 1901

Thymoquinone in wild bergamot oil.

Ph. Rev., 19, p. 200.

Upon purification of non-phenol portion of oil distilled from *M. fistulosa* with water vapor, yellow crystals separated in the condenser and were identified as thymoquinone. The first mention of the isolation of thymoquinone from a volatile oil. Relation of thymoquinone to cymene and carvacrol, both found in the oil.

Quinhydrone hypothesis of plant pigmentation advanced.

Branndel, I. W. and Kremers, E. 1901

Hydrothymoquinone in wild bergamot oil.

Ph. Rev., 19, p. 244.

Hydrothymoquinone, m. p. 140, separated from the phenol portion of the oil of *Monarda fistulosa.*

Formation of thymoquinhydrone from hydrothymoquinone and thymoquinone.

Application of quinhydrone hypothesis of plant pigmentation.

Beck, J. J. 1903

Oil from the corolla of Monarda fistulosa.

Ph. Rev., 21, p. 111.

The probability of the purple color of the corolla and the stem of *M. fistulosa* being due to thymoquinhydrone.

The dried corollas of *M. fistulosa* when distilled with steam yielded 2.71 per cent of a dark reddish brown oil. Sp. gr. 0.9586 indicating a high percentage of carvacrol and its oxidation products. Responded to Flueckiger's test for carvacrol.

Brandel, I. W. 1903

Oil from the leaves of Monarda fistulosa.

Ph. Rev., 21, p. 113.

The oil obtained by distilling the green leaves, stripped from the stem, was almost colorless possessing in some degree the straw yellow color of carvacrol. Sp. gr. 0.9241 at 20°, angle of rotation 0°–9′.

Brandel, I. W. and Kremers, E. 1903

Oil of Monarda didyma.

Ph. Rev., 21, p. 109.

100 lbs. of "Oswego tea" yielded 14 cc of oil when distilled with steam or about 0.03 per cent. Light reddish brown in color, sweetish balm like odor. Sp. gr. 0.902. Angle of rotation + 10°. No test for phenol.

Brandel, I. W. 1904

The volatile oil from Monarda citriodora.

Ph. Rev., 22, p. 153.

The dried flowering herb of *Monarda citriodora* obtained from Dallas, Texas, when distilled yielded about 1 per cent of oil. Sp. gr. 0.9437 at 20°. Phenol assay revealed presence of 65.6 per cent of phenol. Aldehyde present calculated as citral equaled 1.2 per cent. Hydrothymoquinone isolated from phenol oil. Phenol identified as carvacrol.

Rabak, F. 1904

Oxidase from Monarda fistulosa.

Ph. Rev., 22, p. 190.

The isolation of a ferment from *Monarda fistulosa* which oxidises hydrothymoquinone to thymoquinone with the formation of the intermediate product, thymoquinhydrone. Application of the quinhydrone pigmentation hypothesis.

Action of the oxidase tried upon cymene and menthol with negative results.

Swingle, D. B. 1904

The thermal "death-point" of the Monarda ferments.

Ph. Rev., 22, p. 193.

The Monarda ferments when heated for ½ hour to 76–77° gave no reaction with guaiac, to 80–81° no action with either guaiac or H_2O_2.

Wakeman, N. 1908

Quantitative determination of oxidase in the leaves of Monarda fistulosa.

Ph. Rev., 26, p. 314.

The results of weekly determinations of the amount of oxidase in the leaves of *M. fistulosa*, by measuring the amount of oxygen liberated with H_2O_2. The young leaves at the top of the plant were found to yield the most oxidase, while old leaves and the blossoms gave a comparatively slight reaction.

Schimmel & Co. 1908

Oil of Monarda didyma L.

Report S. & Co., Nov. 1908, p. 89.

Half faded blossoms yielded 0.32 per cent of pale yellow oil, rich in paraffin, difficultly soluble in alcohol 20 vols. 70 per cent.

Almost dry stalks and leaves yielded 0.096 per cent of lemon yellow colored oil more soluble in alcohol, 2 or more volumes.

Odor of two oils lavender-like.

Schimmel & Co. 1909

Oil from Monarda didyma L.

Ber. S. & Co., Oct. 1909, p. 80.

An oil distilled from the half withered flowers of *M. didyma* had the following constants: d15° 0.8740, $[a]_D = -15° 45'$, $N_d 20° = 1,467.43$. Acid number 4, 6, Ester number 5, 6.2. Soluble in 3 or more volumes 70 per cent alcohol. After the addition of 6 volumes of alcohol the separation of paraffin took place. Color lemon-yellow, faint odor of ambergris.

Wakeman, N. 1910

The higher oxidation products of thymoquinone.

Proc. Am. Ph. Assn., 58, p. 979.

A study of the oxidation products of thymoquinone giving methods of preparation and physical and chemical properties, with complete bibliography; also their occurrence in the Monarda species.

L Soc 4707.55

BULLETIN OF THE UNIVERSITY OF WISCONSIN
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THE CLASSIFICATION OF CARBON COMPOUNDS

BY

EDWARD KREMERS, PH. D.
Professor of Pharmaceutical Chemistry
The University of Wisconsin

CONTRIBUTIONS FROM THE COURSE IN PHARMACY

MADISON, WISCONSIN
1912

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PREFATORY REMARKS

> **"Arbeit allein kann die Licht gebenden Ideen nicht herbeizwingen. Etwas vom Schauen des Dichters muss auch der Forscher in sich tragen."**
>
> **Helmholtz.**

> **"La science ne consiste pas en faits, mais dans les conséquences que l'on en tire."**

At the annual meeting of the Wisconsin Academy of Sciences, Arts, and Letters in December, 1894, the writer read a paper "On the classification of carbon compounds" which was published in the Transactions[1] of that body. The introductory paragraph may here be quoted:

"In the winter semester of 1888–9, Professor August Kekulé, in his course on the chemistry of the carbon-compounds at the University of Bonn, Germany, introduced the subject of fatty alcohols, aldehydes, ketones, acids, hydroxy acids, etc., by a lecture in which he gave a general survey of the theoretically possible hydroxy derivatives of the paraffin hydrocarbons. I suppose it was Prof. Kekulé's usual method of treating the subject, but I am not warranted in making so broad a statement. However, this theoretical introduction is fully in harmony with the methods of teaching of this genial lecturer, known and celebrated not so much for the compounds he has discovered, but for his theories, that have prophesied the possibility of hosts of compounds, which have been prepared by others in the attempt to establish as well as in the attempt to overthrow Prof. Kekulé's theories."

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[1] **Vol. 10, p. 310. A second paper was read ten years later, but not published. At the Baltimore meeting of the American Chemical Society in 1909 a twenty-minute paper on the same subject was read by request at a general meeting of the Association.**

If honest confession be good for the soul, the above paragraph ought to suffice to show that the writer makes no great claim for originality and at the same time it reveals the source of his inspiration. All that the writer claims is that he has endeavored to systematize by means of logical questions and answers.

The problem of rational classification of the carbon compounds is one of those that can not be worked out in the research laboratory, but has to be solved primarily in the class room. Now, that after more than twenty years of experience in this direction the system has revealed its advantages not only in the class room of the writer but in the class rooms of his former students as well, the time seems to have arrived when the more completely worked out system should be given wider publicity.

However, while the system had to be tried out in the classroom, the conference, and the seminar, it has found useful application in laboratory research. As applied to the sesquiterpenes,[2] as representatives of the hydrocarbons, it has evidently proven acceptable to others.[3]

In the systematic study of the glucosides, pigments, and alkaloids it has brought out relationships formerly not apparent. An attempt is also being made to make the organic laboratory manual something more than a collection of working formulas, and suggestions for reading. As to details, the writer hopes to find the time to bring the entire *materia phytochemica* into conformity with this system and thus to show the numerous practical as well as theoretical advantages which it possesses.

It may be suggested that the time is not opportune for a revision of the classification of carbon compounds on the basis of structural atomic chemistry, since the atoms are about to be replaced, in chemical thought, by electrons. Such a suggestion, however, is not likely to be well received so long as even physicists warn chemists "not to be too ready to throw away conceptions (such e. g. as that of an atom) . . . that have proved very valuable as aids to the advancement of science in the past."[4]

---

[2] O. Schreiner, *The sesquiterpenes*, p. 17.

[3] Comp. *"Neuere Eintheilung der Sesquiterpene"* in Arnold Lewinsohn, *Beitraege zur Kenntniss der Sesquiterpene, Innaugural-Dissertation*, Leipzig, 1908, p. 14.

However valuable the theory of electrons may prove, it may be a generation or more before it can affect our ideas of the classification of carbon compounds, should it ever exert such an influence. While we should always welcome new tools and learn to use them if possible, it would be foolish indeed to discard an old tool, simply because a new one, which we have not learned to use, is in sight.[5]

All that the writer asks for the suggestions toward the rational classification of the carbon compounds is that they be given a fair trial. He fully realizes that in such matters changes are not likely to come about with revolutionary suddenness, but that old habits of thought must be gradually overcome by the slow process of evolution.

DEFINITION OF ORGANIC CHEMISTRY

For the purpose of this study organic chemistry is defined as the chemistry of the hydrocarbons and their substitution products. Not that this definition covers ground other than that covered by the definition mostly in vogue at the present time, *viz.*, that organic chemistry is the chemistry of the carbon compounds, but that the definition suggested has this advantage in the study of classification and nomenclature that it emphasizes two important lines of thought and development. First, it emphasizes the fact that the hydrocarbons, the simplest of carbon compounds, are to be regarded as basal compounds and that all other carbon compounds are to be derived from these hydrocarbons by the process of substitution.

---

[4] President Richard G. Mac Laurin of Mass. Inst. of Techn. at the banquet of the A. C. S. Science, 32, p. 10.

[5] It would be more than foolish for the accomplished piano player to abandon his instrument at the age of twenty-five or more because he has become convinced that the violin is the more perfect musical instrument. While a successful pianist, he might, and, in all probability, would, achieve only mediocrity with the violin. The same reasoning applies to the present day chemist and his *possible change from the atomic to the electron theory.*

Kolbe at one time suggested that all carbon compounds be derived from carbon dioxide from which the plant synthesizes its complex carbon compounds. But though we could follow the synthetic processes of the plant much better than we can even today, no one would any longer think of following such a suggestion for purposes of classification or nomenclature. Our knowledge of the hydrocarbons, however, is such that today they universally serve as the basal compounds, not only for purposes of classification and nomenclature but for didactic purposes as well. What we need at present is a more rational classification of these basal hydrides of carbon than is commonly found in organic chemical literature.

The second basal thought suggested by the definition is, as already pointed out, that all other carbon compounds be derived from the hydrocarbons by the process of substitution. In research work, in preparation work, and also in analytical processes we make extensive use of the additive capacity of compounds.

We need in no wise underestimate the importance of the addition product because addition is not universally applicable, yet this is more than sufficient reason for not adopting it as a basal process in a system of classification and nomenclature. Neither can we for this purpose adopt advantageously any other than a unitarian point of view. What we need in organic classification and nomenclature is to get rid, for the purpose under consideration, of points of view based on totally different conceptions, such as the old dualistic view of acids, bases, and salts, that of the theory of types, etc.

The term organic chemistry is said to have been introduced by Bergmann who pointed out that there was no fundamental difference between the chemical compounds from the vegetable and animal kingdoms. Previous to his time the materia chemica, and with it chemical science, was divided according to the source of the material from the mineral, vegetable, and animal kingdoms. In this chemists had followed the suggestion by

Emanuel, who in 1682 classified all terrestrial objects according to their relation to one of these natural kingdoms. However, organic chemistry was long thereafter still subclassified into vegetable chemistry and animal chemistry.

The student of organic chemistry is usually told that by his so-called synthesis of urea, Woehler in 1828 dealt the death-blow to the notion that organic chemistry is the chemistry of the functions of organs and their products, in other words of that mysterious something called life. Yet Woehler's so-called synthesis was no synthesis at all, but an inversion, an intramolecular re-arrangement of the atoms of one molecule to another of like size. Neither did Woehler's noteworthy and far-reaching observations immediately influence chemical thought, at least so far as definition and classification reflected the advance of chemical thought. Even Gmelin stated that "the bodies of the organic kingdom are distinguished in their most complete state, from those of the inorganic kingdom . . . by being composed, for the principal and most important part at least, of chemical compounds quite peculiar to them, called organic compounds . . ."[1]

Today we have gotten away completely from any significance of life so far as the concept organic chemistry is concerned. That branch of chemistry which deals with the so-called life processes of plants and animals is termed biochemistry and represents a line of chemical activity as does phytochemistry and zoochemistry. Organic chemistry is universally interpreted at present as implying the chemistry of the carbon compounds irrespective of source or mode of formation. The term carbon has reference to elemental composition and could not have been used before the recognition of the modern elements since the close of the 18th century. Indeed, its use in the sense as quoted above is of much more recent date. The first to have suggested the definition of organic chemistry as the chemistry of carbon, appears to have been Gerhardt as early as 1844 or possibly earlier.[2] Kekulé then suggested that we "define organic chemistry as the chemistry of the carbon compounds."[3] This definition-subtitle was accepted by Richter, one of the disciples of Kekulé and author of the well known text which has been repeatedly revised by Anschuetz and translated into English by Smith.[4]

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[1] For a more detailed statement see Appendix: *Definitions of organic chemistry.*

[2] See Appendix: *Definitions of organic chemistry.*

As a mere definition this will do as well as any other, especially if interpreted in the light of Kekulé's commentary,[5] but if our definition is to point logically to the method of classification, as the classification should reflect the most satisfactory chemical theories, then it is no longer satisfactory for purposes such as are here to receive consideration. Hence for our present needs we prefer to define organic chemistry as the chemistry of the hydrocarbons and their substitution products. A careful perusal of the principles of classification will, no doubt, be found to justify the adoption of this definition which is equally valuable from a didactic point of view.

HISTORY OF ORGANIC CHEMICAL CLASSIFICATION

In order to give proper expression to chemical ideas, a chemical language has been developed which reflects chemical thought. Science, we are told, consists not of facts, but in the conclusions which we draw from them. Some of the most important conclusions drawn from chemical facts have been derived by systematization of the *materia chemica*. As a result, general theory and chemical classification have developed side by side, so that the study of the history of classification reflects in no small part the advance made in general chemical theory.

A review of the principal systems of classification of the past hundred years and more, clearly reveals the fact that the rational systems of classification were based largely on structural theories, structural of necessity, in the varying sense in which this concept was interpreted from time to time. The temporary breakdown of structural conceptions during the middle of the nineteenth century, when atoms had to give way to equivalents, gave rise to a condition bordering on anarchy not only in classification but in general chemical thought. The arrangement of carbon compounds according to the number of carbon atoms* is no more a rational classification than the arrangement of plants according to the number of the stamens of their flowers. Such an artificial arrangement, while of value in the tracing of analytical results based on elementary analysis[1] does not afford for most purposes even the convenience of the alphabetical arrangement of the chemical dictionary or encyclopedia.

---

[3] See Appendix: *Definitions of organic chemistry.*

[4] Victor von Richter's *Organic Chemistry or Chemistry of the Carbon Compounds*. Edited by R. Anschuetz. Authorized translation by E. F. Smith, 1899.

[5] See Appendix: *Definitions of organic chemistry.*

Previous to the chemistry of oxygen, as elucidated by Lavoisier, there was no organic chemistry in name, and but few carbon compounds had been isolated or prepared artificially.[2] Yet in order to understand later developments, it seems advisable to go back as far as Lemery and one of the first chemical texts free from alchemistic jargon, his *Cours de chimie.*

Following the classification of all natural objects (and beings) into three natural kingdoms, the *regna naturae,* suggested by Emanuel in 1682, Lemery arranged the subject matter of his Course in Chemistry under these headings:

1.) Upon minerals
2.) Upon vegetables, and
3.) Upon animals.

As early as 1780, Bergmann began to distinguish organic from inorganic bodies, having shown that the same organic substances can be obtained from both the vegetable and animal kingdoms. Nevertheless, the classification of the organic *materia chemica* according to the two kingdoms of organized nature, namely the vegetable and animal was upheld for a long time.

Thus Lavoisier, whose principal point of view was that of oxygen first, last, and all the time, separates the carbon-containing acids obtained from the vegetable kingdom from those obtained from the animal kingdom. This separation is found even in the third, rewritten and revised edition of Lavoisier's "*Traité élémentaire de chimie*" of 1801.

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* See Appendix: Arrangement according to number of carbon atoms.

[1] Compare Richter's Lexikon der Kohlenstoff-Verbindungen, and the Formelregister of the Berichte der deutschen chemischen Gesellschaft based on the same principle.

[2] See Appendix: Classification as revealed by tables of contents.

Fourcroy, one of Lavoisier's associates on the Commission of Chemical Nomenclature according to the antiphlogistic system, likewise distinguished between "*les composés végétaux*"[3] and the "*substances animales.*"[4]

Berzelius, the great generaliser of his time, in his epoch-making "*Lehrbuch der Chemie*" does likewise, even in the third edition published in 1837. His organic chemistry is subdivided into "*Plant Chemistry*"[5] and "*Animal Chemistry.*"[6]

With such classical examples as guides, it is not surprising that other authors folowed even up to the middle of the nineteenth century. Thus this system of classification long outlived its theoretical usefulness.

Whatever may be said for or against the designation of Lavoisier as the founder of chemical science, this much is undeniably true that his antiphlogistic theories placed chemical classification and nomenclature on a new basis. As already pointed out, the chemistry of Lavoisier was the chemistry of oxygen just as the predominant chemistry of Kekulé and of the generation of chemists that followed him was a chemistry of carbon, even more so. The oxides of the metals were designated bases, the oxides of the nonmetals, acids, both binary compounds, and the union of the two resulted in the ternary compounds or salts which naturally also contained oxygen. Thus there was laid the foundation for the electrochemical theories of Davy and the dualistic structural theories of Berzelius. The discovery of the halogens and their derivatives naturally modified these views but they did not revolutionize them. Indeed we today are still under the ban of the antiquated theory of acid, base and salt.

Compared with the inorganic field, organic chemistry as defined by Bergmann played but a minor role though it was being enriched by Scheele and other phytochemists. Yet organic chemistry had its organic acids comparable to the inorganic acids, it also had its inorganic salts of these organic acids. The organic base, however, was wanting until Sertuerner discovered it in morphine, this "new salifyable plant base" as he called it. This morphine attracted universal attention, not because it had been isolated from opium, for such isolation had been effected independently by both Derosne and Sertuerner more than a dozen years before, but because Sertuerner had recognized its basic, i. e. its salt-forming properties. Thus the parallel between organic chemistry and inorganic chemistry was thought to have been established.

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[3] Systeme des connaissances chimique (Bumaire, An. IX), tomes 7 et 8.
[4] Ibidem, tomes 9 et 10.
[5] Vols. 6, 7 and 8 of the 3rd German edition of 1837.
[6] Vol. No. 9 of the same edition.

This satisfaction, however, was of but short duration for chemists soon realized the importance of the fact, already hinted at by Sertuerner, that morphine and the alkaloids discovered in rapid succession, were related to the inorganic ammonia, rather than to the oxygen bases of the metals.

The conception of this parallel, however, seemed too good to be abandoned, so it was revived by Liebig who pointed out that the organic alcohol was the true analogue of the inorganic base as the organic acid was that of the inorganic oxygen acid. In like manner the product of the union of organic acid and alcohol, the etheral salt or ester, was regarded as the analogue of the inorganic salt. Thus there was re-established the true analogy between organic chemistry and inorganic chemistry, and organic chemistry was defined the chemistry of the compound radicle by Liebig, the alkyl or positive radicle corresponding to the metal, the acyl or negative radical to the non-metal. Whereas the difficulties of the inorganic system were patched up by coining new names, such as halogen acids and halides, thioacids and thionates, the difficulties of the organic field would not be downed by coining such words as neutral principles, i. e. substances that were neutral in themselves and not by virtue of the neutralizing power of acid upon alkali or vice versa. Yet in organic chemistry as in inorganic chemistry we are still laboring under the ban of opposites, of acids and alcohols, which instead of being regarded primarily as opposites should rather be looked upon as related compounds.

The difficulties arising from the ever growing number of carbon compounds were not solved by creating new classes of compounds or by relegating them to an ever convenient lumber chamber. The conception of the rigid radicle, this element, so-called, of organic chemistry, had to be abandoned in the light of the theory of substitution. The concept of homology, though it aided materially in throwing light on difficult problems, did not remove the more fundamental difficulties of the situation. Neither did the theory of types, though it, more than any one other conception, aided in bringing order into chaos, and though it paved the way for the structural theories of Kekulé.

All of these theories and views are reflected in chemical nomenclature and classification. These reflections are found not only in the chemical history of the past century, but in our present day mode of chemical thought and language. While useful at times, they often linger as an obstructing *"spuk,"* just as the life *"spuk"* of organic chemistry has made its presence felt again and again and has not been downed completely even today. The manner in which these ideas are reflected in chemical classification can best be seen from the tables of contents of contemporary treatises on chemistry.

The structural conceptions of Kekulé are too well known to be reviewed here. How he arrived at them he himself has told us in his after dinner speech of 1890 at the celebration of the twenty-fifth anniversary of the benzene theory.[7] How he worked out his structural or graphic formulas is best shown in some of the considerations of the next chapter.

Frankland having recognized the tetravalence of the carbon atom, Kekulé added the type methane to the older types ammonia, water, hydrohalogen and hydrogen. The structural conception of the hydrocarbons of the methane series and of their halogen and hydroxy substitution products resulted. These, together with the olefine and acetylene hydrocarbons and their respective derivatives were grouped together as fatty compounds. His conception of the structure of benzene added still a new type and its homologues and their derivatives were grouped together as aromatic compounds.

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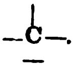
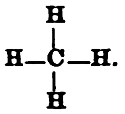
[7] *Berichte*, 23 p. 1306. For an English translation see the Kekulé lecture by Jepp in the J. C. S. 73 p. 100 of Transactions.

Great as was the advance made by Kekulé in his classification there is today no more justification in adhering to it than to the notion of acids and bases. Both conceptions emphasize opposites whereas the relation of gradual evolution is the important point to be emphasized. Opposition becomes apparent only when we take two compounds or classes of compounds out of their natural surroundings and contrast them by ignoring the intervening links. In an age of evolution such a method of procedure is as fundamentally wrong in chemistry as it is in biology.

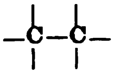
A PROPOSED BASIS FOR THE RATIONAL CLASSIFICATION OF CARBON COMPOUNDS

CLASSIFICATION OF THE HYDROCARBONS

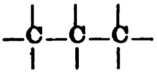
Assuming the tetra-valence of the carbon atom, there is but one hydrocarbon in which all four of the affinities of the carbon atom can be saturated by hydrogen. The four affinities may be indicated in the plane of the printed page by four lines in the following manner:  $\overset{|}{\underset{|}{-\mathrm{C}-}}$. If these affinities are saturated by hydrogen we get the formula for methane or marsh gas, CH_4 or



$\mathrm{H}-\overset{\overset{\mathrm{H}}{|}}{\underset{\underset{\mathrm{H}}{|}}{\mathrm{C}}}-\mathrm{H}$. In place of saturating these four affinities with hydrogen, or *e. g.*, with halogen or oxygen, it may be assumed that one or more may be satisfied by the same number of valencies of other carbon atoms. Assuming for the present that the carbon atom be united with other carbon atoms by single affinities only, we get the following carbon nuclei with their free affinities:



$-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-$



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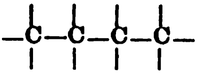
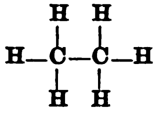
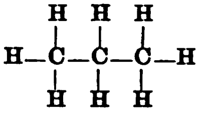


$-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-$

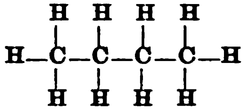
If these free affinities are now satisfied by hydrogen, the following hydrocarbons result:



$$\mathrm{H}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\mathrm{H}$$



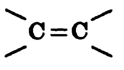
$$\mathrm{H}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\mathrm{H}$$

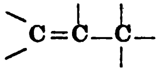


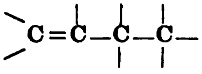
$$\mathrm{H}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\underset{\mathrm{H}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\mathrm{H}$$

, It will be seen at once, that each carbon atom is united with two hydrogen atoms, and that the two end carbon atoms have a third affinity satisfied by hydrogen. For n carbon atoms there are, therefore, 2n + 2 hydrogen atoms in each molecule. Hence, the general formula for these and like hydrocarbons will be $C_n H_{2n+2}$. Having assumed a tetra valence for the carbon atom this will, therefore, be the limit series of hydrocarbons (*Grenzkohlenwasserstoffe*). We can imagine but one such series and only one is known.

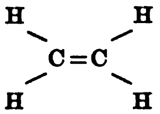
If in place of uniting two carbon atoms of the same molecule by a single bond, we imagine them united by two bonds the following carbon nuclei will result:

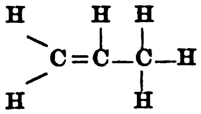


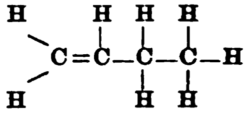




If the free affinities be now satisfied by hydrogen atoms the following hydrocarbons are obtained:





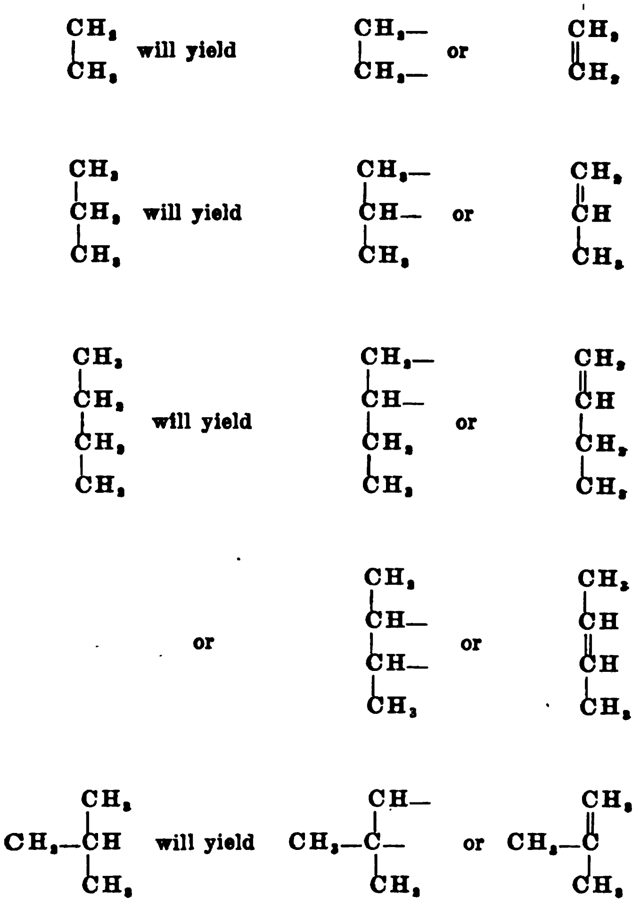


The addition of the carbon and hydrogen atoms in each molecule will show that these hydrocarbons contain two hydrogen atoms less than the hydrocarbons with the same number of carbon atoms first developed. Their general formula will, therefore, be:

$$C_n H_{2n+2} - H_2 = C_n H_{2n}.$$

Hence we can derive the hydrocarbons of the formula C_nH_{2n} from the hydrocarbons of the formula C_nH_{2n+2} by the abstraction of two hydrogen atoms.

This abstraction of hydrogen atoms may take place first of all in connection with neighboring carbon atoms. Thus



$$\begin{array}{c} CH_3 \\ | \\ CH_3 \end{array} \text{ will yield } \begin{array}{l} CH_2— \\ | \\ CH_2— \end{array} \text{ or } \begin{array}{c} CH_2 \\ \| \\ CH_2 \end{array}$$

$$\begin{array}{c} CH_3 \\ | \\ CH_2 \\ | \\ CH_3 \end{array} \text{ will yield } \begin{array}{l} CH_2— \\ | \\ CH— \\ | \\ CH_3 \end{array} \text{ or } \begin{array}{c} CH_2 \\ \| \\ CH \\ | \\ CH_3 \end{array}$$

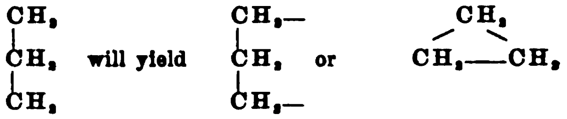
$$\begin{array}{c} CH_3 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ CH_3 \end{array} \text{ will yield } \begin{array}{l} CH_2— \\ | \\ CH— \\ | \\ CH_2 \\ | \\ CH_3 \end{array} \text{ or } \begin{array}{c} CH_2 \\ \| \\ CH \\ | \\ CH_2 \\ | \\ CH_3 \end{array}$$

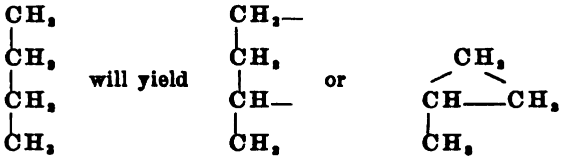
$$\text{or } \begin{array}{l} CH_3 \\ | \\ CH— \\ | \\ CH— \\ | \\ CH_3 \end{array} \text{ or } \begin{array}{c} CH_3 \\ | \\ CH \\ \| \\ CH \\ | \\ CH_3 \end{array}$$

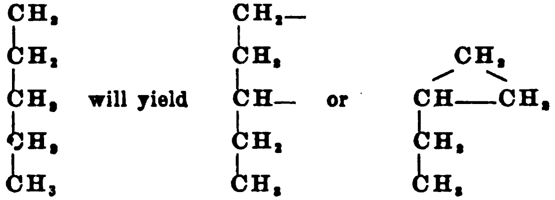
$$\begin{array}{c} \quad CH_3 \\ \quad | \\ CH_3—CH \\ \quad | \\ \quad CH_3 \end{array} \text{ will yield } \begin{array}{c} \quad CH— \\ \quad | \\ CH_3—C— \\ \quad | \\ \quad CH_3 \end{array} \text{ or } \begin{array}{c} \quad CH_2 \\ \quad \| \\ CH_3—C \\ \quad | \\ \quad CH_3 \end{array}$$

These hydrocarbons are identical with those derived by the previous method.

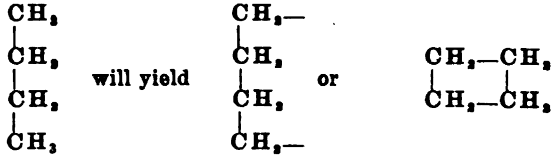
Secondly, the two hydrogen atoms may be abstracted from carbon atoms that are not neighboring but have one other carbon atom intervening. In that case

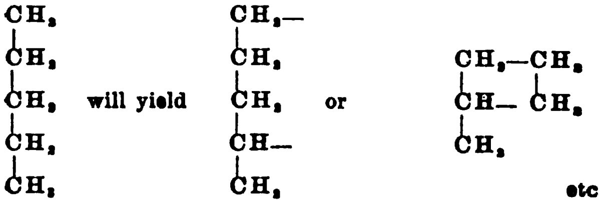






If next we allow two carbon atoms to intervene between the carbon atoms from which the hydrogen atoms are abstracted the following cyclic hydrocarbons result:



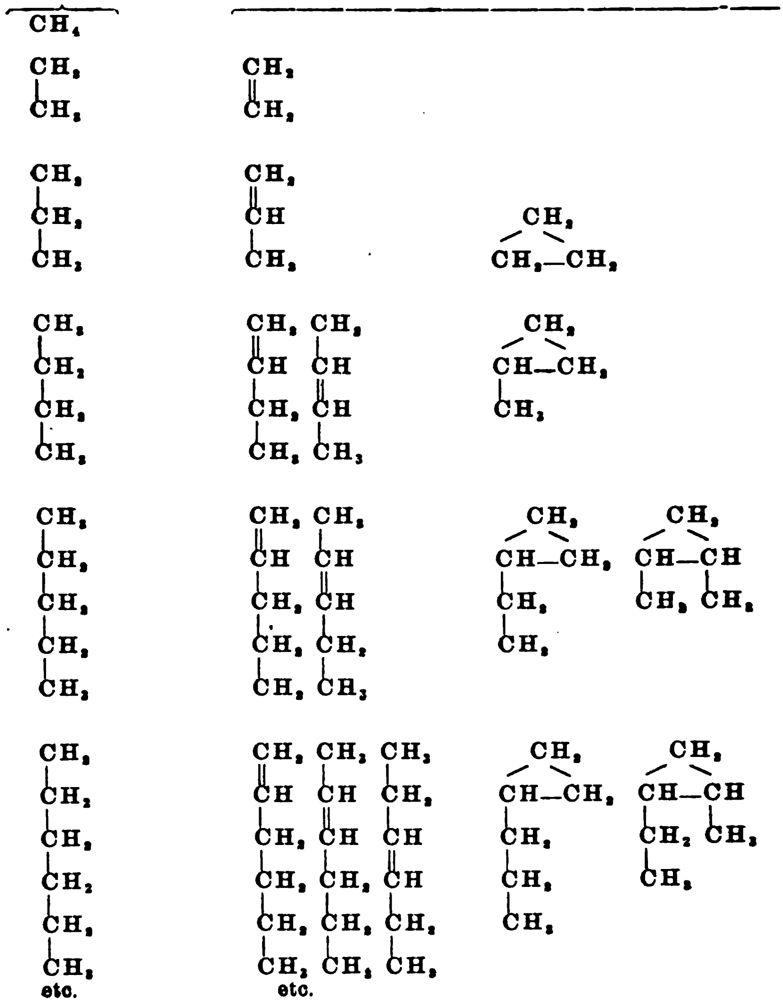


etc.

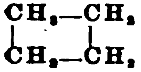
Next we may allow three, four or more carbon atoms to intervene and cyclic hydrocarbons with five, six and more members to the cycle will result.

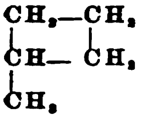
Proceeding from normal hydrocarbons of the methane series the following hydrocarbons are obtainable. The cyclic members are classified according to the number of carbon atoms to the cycle and are tabulated so as to show the isomerism of the hydrocarbons with the same number of carbon atoms.

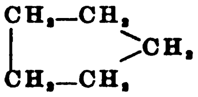
C_nH_{2n+2}

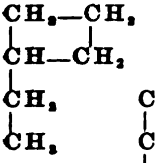


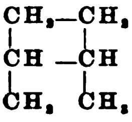
C H_{2n}

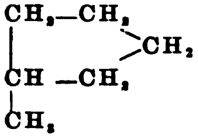


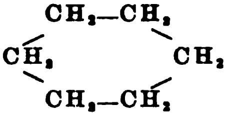












A second dimethyl cyclobutane has been omitted for want of space.

Whereas of the formula of saturation C_nH_{2n+2} but one series of hydrocarbons is possible, and representatives of but one series are known; of the formula of saturation $C_n H_{2n}$, one chain series and an indefinite number of cyclic series can be developed. Representatives of the chain series and of four of the cyclic series are known. Derivatives of still another series with seven carbon atoms to the cycle are likewise known.

The names of the normal chain hydrocarbons and initial members of the cyclic series are commonly given in accordance with the principles of the Geneva Congress.

If we now proceed one step farther and abstract two more hydrogen atoms we arrive at the formula of saturation C_nH_{2n-2}. Under this formula two unsaturated chain series and the following unsaturated monocyclic series and saturated dicyclic series may be developed.

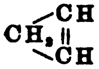
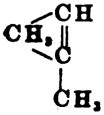
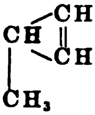
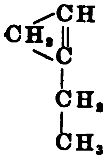
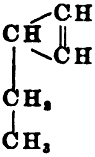
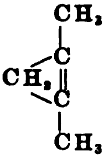
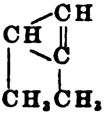
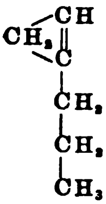
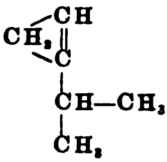
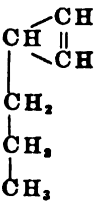
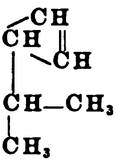
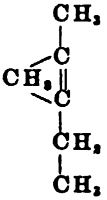
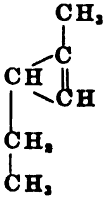
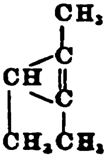
In the following tabulations some of the isomeric forms have been omitted for want of space on the page on which they belonged. All isomeric forms with the double bonds in the side chains have been omitted for the same reason. These tables have been compiled, not with any idea of completeness, but rather for the purpose of affording a convenient oversight such as seems necessary for a proper grasp of the situation.

C_nH_{2n-2}

≡	= =
$CH\equiv CH$	
$CH\equiv C-CH_3$	
$CH\equiv C-CH_2-CH_3$ $CH_3-C\equiv C-CH_3$	$CH_2=CH-CH=CH_2$
$CH\equiv C-CH_2-CH_2-CH_3$ $CH_3-C\equiv C-CH_2-CH_3$	$CH_2=CH-CH=CH-CH_3$ $CH_2=CH-CH_2-CH=CH_2$
$CH\equiv C-CH_2-CH_2-CH_2-CH_3$ $CH_3-C\equiv C-CH_2-CH_2-CH_3$ $CH_3-CH_2-C\equiv C-CH_2-CH_3$	$CH_2=CH-CH=CH-CH_2-CH_3$ $CH_2=CH-CH_2-CH=CH-CH_3$ $CH_2-CH=CH_2-CH_2-CH=CH_2$ $CH_3-CH=CH-CH=CH-CH_3$

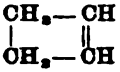
C_nH_{2n-2}

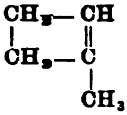
Γ Δ

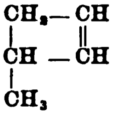
		
		
		 
 	 	  

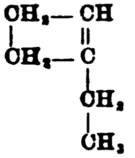
C_nH_{2n-2}

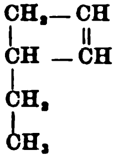
Γ Δ

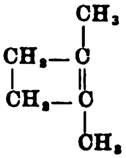


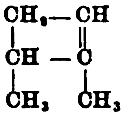


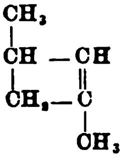




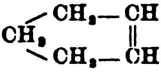
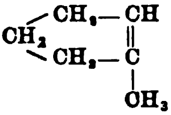
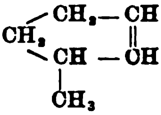
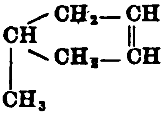
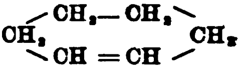






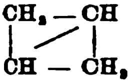


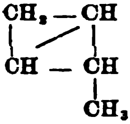
C_nH_{2n-2}

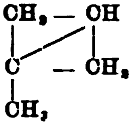
Γ Δ	
	
  	

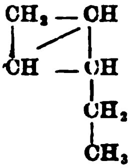
C_nH_{2n-2}

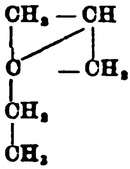
△ △

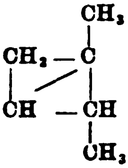


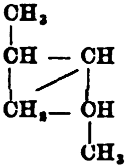


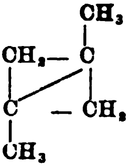




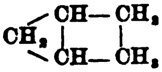
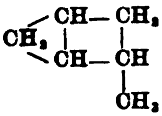
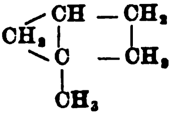
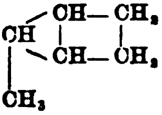
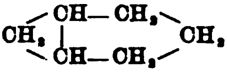
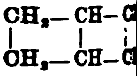








C_nH_{2n-2}

△ △	
	
  	 

It is not necessary to carry the details of this process any farther, if we but realize the important conclusion that can be derived from the few instances cited, *viz.*, that the structural equivalent of two hydrogen atoms is either a double bond or a cycle, also that in place of two double bonds we may have still another structural equivalent, the treble bond.

Bearing this in mind, we can readily classify under each formula of saturation the groups of series of hydrocarbons. In the following table these groups are indicated with the use of the following symbols:

Γ = double bond
△ = cycle
Ϝ = treble bond.

C_nH_{2n+2}	C_nH_{2n}	C_nH_{2n-2}	C_nH_{2n-4}
	Γ	Γ Γ	Γ Γ Γ
	△	Γ △	Γ Γ △
		△ △	Γ △ △
			△ △ △
		Ϝ	Ϝ Γ
			Ϝ △

C_nH_{2n-6}	C_nH_{2n-8}	C_nH_{2n-10}	C_nH_{2n-12}
Γ Γ Γ Γ			7 Γ
Γ Γ Γ △			6 Γ and 1 △
Γ Γ △ △			5 Γ and 2 △
Γ △ △ △			etc.
△ △ △ △			
Ϝ Ϝ			
Ϝ Γ Γ			
Ϝ Γ △			
Ϝ △ △			

Hence, the hydrocarbons may be rationally classified
Firstly, According to their degree of saturation;
Secondly, According to their chain or cyclic character;
Thirdly, According to the number of carbon atoms.

CLASSIFICATION OF THE SUBSTITUTION PRODUCTS OF THE HYDROCARBONS

Having outlined very briefly, the principles that should govern us in a rational classification of the basal carbon compounds, the hydrocarbons, we are now prepared to classify their substitution products.

In the large number of known hydrocarbons and in the thousands of unknown but possible hydrocarbons we have, in addition to carbon atoms that have their four affinities saturated exclusively with the affinities of other carbon atoms, the following three simple hydrocarbon groups:

$—CH_3$, the univalent methyl group
$=CH_2$, the bivalent methylene group
$\equiv CH$, the trivalent methenyl or formyl group

As has already been pointed out, methane constitutes the single exception to this rule. Hence its substitution products or derivatives differ somewhat from the analogous derivatives of other hydrocarbons.

Inasmuch as we are going to regard all carbon compounds as substitution products, direct or indirect, of the underlying hydrocarbons, all direct substitution must take place in connection with one of these three simple groups. This suggests at once one of the basal ideas of classification.

Even more fundamental, however, is the conception of how often substitution has taken place. Inasmuch as it is the univalent hydrogen of the hydrocarbon that is replaced step by step, the unit of substitution must be a univalent atom or radicle. Accordingly we distinguish between mono-, di-, tri-, tetra-, etc. substitution products. This is done irrespective of the substituting element or radicle.

In order to illustrate the principles involved, substitutions with univalent elements also with the univalent hydride radicles of divalent and trivalent elements will be effected.

HALOGEN SUBSTITUTION PRODUCTS

For substitution with a univalent element, the halogens are best adapted. Of mono-halogen substitution products there must be three types, since all three simple hydrocarbon groups contain at least the one hydrogen atom necessary for mono-substitution.

$-CH_3$	$-CH_2X$
$=CH_2$	$=CHX$
$\equiv CH$	$\equiv CX$

Whereas mono-substitution can take place only in connection with one carbon atom, di-substitution can take place in connection with either one or two carbon atoms. If it takes place in connection with the same carbon atom, two types of di-substitution products are possible, and only two, for but two of the three simple hydrocarbon groups contain the requisite two hydrogen atoms, *viz.*

$-CH_3$	$-CHX_2$
$=CH_2$	$=CX_2$

Tri-halogen substitution can take place in connection with one, two or three carbon atoms. If it takes place in connection with the same carbon atom, but one type of tri-halide is possible, since but one of the three simple hydrocarbon groups contains the requisite number of hydrogen atoms to admit of tri-substitution, *viz.*

$-CH_3$	$-CX_3$

With the exception of methane, which, with its derivatives, as has already been pointed out, must occupy an exceptional position in any rational classification, tetra-substitution cannot take place in connection with one and the same carbon atom. Hence the possibilities of substitution in connection with one and the same carbon atom are exhausted with tri-substitution. Substitution in connection with different carbon atoms will be considered later. Suffice it for the present to state that no new types are created by substitution in connection with different carbon atoms. The isomerism thus produced is one of position. The influence of position on the structure of a molecule is a study by itself and should not be confounded with that of simple types.

HYDROXY SUBSTITUTION PRODUCTS

Among the divalent elements of organic chemistry, oxygen is undoubtedly the most important. Inasmuch as the unit of substitution in the underlying hydrocarbon is the univalent hydrogen atom, it would not be rational to replace, step by step, hydrogen atoms by their oxygen equivalents. Substitution, however, can be rationally effected by a univalent oxygen-hydrogen radicle, such as we possess in the hydroxy or hydroxyl group, *viz.* the (-O-H).

The simplest kind of hydroxy substitution product will naturally be the mono hydroxide. As of mono-halides, and for the same reason, there are three types of mono-hydroxides or alcohols. They are represented by the following type formulas:

$-CH_3$	$-CH_2OH$
$=CH_2$	$=CHOH$
$\equiv CH$	$\equiv COH$

Of di-substitution products, in which the di-substitution has taken place in connection with the same carbon atom, two types of dihydroxides, or glycols, are possible, viz.

$-CH_3$	$-CH(OH)_2$
$=CH_2$	$=C(OH)_2$

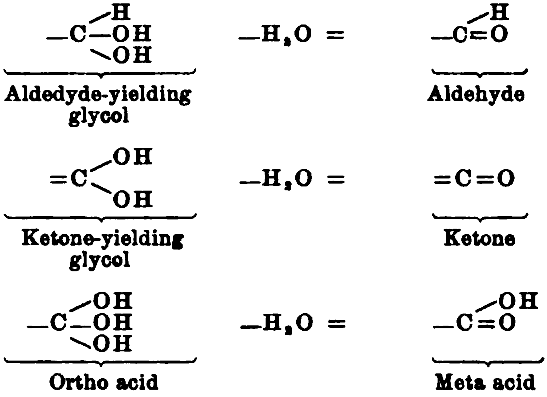
Of tri-hydroxides, in which all three hydroxy groups are connected with the same carbon atom, but one type is possible, *viz.*

$-CH_3$	$-C(OH)_3$

Such a tri-atomic alcohol in which all three hydroxy groups are connected with the same carbon atom is known as an ortho acid.

It is a well known fact in organic chemistry that, whenever two or more hydroxy groups are connected with the same carbon atom, a tendency manifests itself to split off the elements of a molecule of water, a tendency readily interpreted with the aid of the thermochemical equation of water.

The two glycols, also the ortho acid, are subject to such dehydration as indicated by the following type formulas:



$$\underbrace{-C{\begin{array}{l}\nearrow H\\ -OH\\ \searrow OH\end{array}}}_{\text{Aldedyde-yielding glycol}} -H_2O = \underbrace{-C{\begin{array}{l}\nearrow H\\ =O\end{array}}}_{\text{Aldehyde}}$$

$$\underbrace{=C{\begin{array}{l}\nearrow OH\\ \searrow OH\end{array}}}_{\text{Ketone-yielding glycol}} -H_2O = \underbrace{=C=O}_{\text{Ketone}}$$

$$\underbrace{-C{\begin{array}{l}\nearrow OH\\ -OH\\ \searrow OH\end{array}}}_{\text{Ortho acid}} -H_2O = \underbrace{-C{\begin{array}{l}\nearrow OH\\ =O\end{array}}}_{\text{Meta acid}}$$

There are, therefore, as many as nine simple types of oxygen substitution products: six hydroxy substitution products, which, together with their dehydration products are herewith tabulated.

Hydrocarbon groups	Mono-hydroxides	Dihydroxides	Trihydroxides
$-CH_3$ Methyl	$-C{\begin{array}{l}\nearrow H\\ -H\\ \searrow OH\end{array}}$ ..Primary.. alcohol	$-C{\begin{array}{l}\nearrow H\\ -OH\\ \searrow OH\end{array}}$ Aldehyde-yielding glycol	$-C{\begin{array}{l}\nearrow OH\\ -OH\\ \searrow OH\end{array}}$ Ortho acid
		$-C{\begin{array}{l}\nearrow H\\ \searrow\!\!\searrow O\end{array}}$ Aldehyde	$-C{\begin{array}{l}\nearrow\!\!\nearrow O\\ \searrow OH\end{array}}$ Meta acid
$=CH_2$ Methylene	$=C{\begin{array}{l}\nearrow H\\ -OH\end{array}}$ Secondary alcohol	$=C{\begin{array}{l}\nearrow OH\\ \searrow OH\end{array}}$ Ketone-yielding glycol	
		$=C=O$ Ketone	
$\equiv CH$ Methenyl	$\equiv COH$ ..Tertiary alcohol		

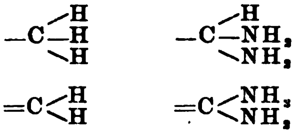
AMIDO SUBSTITUTION PRODUCTS

Of the trivalent elements, nitrogen is unquestionably the most important in organic chemistry. However, it is not practicable to substitute, even in a theoretical way, one-third and two-thirds of a nitrogen atom for one and two hydrogen atoms respectively. The simplest univalent nitrogen-hydrogen radicle, the amido or amino group, however, may replace the hydrogen of an underlying hydrocarbon. As a matter of fact, it is with compounds such as these that the organic chemist has to deal. Hence the nitrogen derivatives can best be studied as amido substitution products and their deammoniated compounds.

As with the halides and hydroxides, the monamides come first. Also, as with the mono-halides and mono-hydroxides, there are three types of monamides, according to the replacement of a methyl, methylene, or methenyl hydrogen atom, as indicated by means of the following formulas:

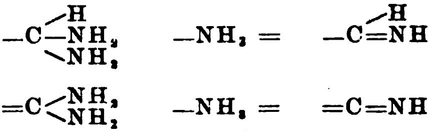
$$\begin{array}{ll} -CH_3 & -CH_2NH_2 \\ =CH_2 & =CHNH \\ \equiv CH & \equiv CNH_2 \end{array}$$

In connection with the diamines we must again distinguish between those diamides in which the two amido groups are connected with the same carbon atom, and those in which they are connected with two carbon atoms. The former only are here considered. Of these there are again two types as of the corresponding di-halides and di-hydroxides, *viz.*



$$\begin{array}{ll} -C\begin{smallmatrix}\diagup H\\ -H\\ \diagdown H\end{smallmatrix} & -C\begin{smallmatrix}\diagup H\\ -NH_2\\ \diagdown NH_2\end{smallmatrix} \\ =C<\begin{smallmatrix}H\\ H\end{smallmatrix} & =C<\begin{smallmatrix}NH_2\\ NH_2\end{smallmatrix} \end{array}$$

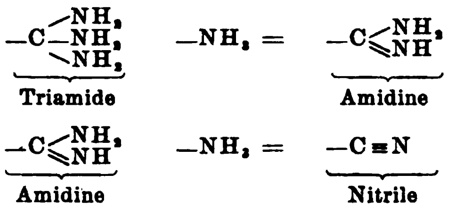
In like manner as the corresponding di-hydroxides readily split off the elements of a molecule of water, so the diamides, (though with less readiness) split off the elements of a molecule of ammonia, yielding the corresponding imides as indicated by the following formulas:



$$\begin{array}{lll} -C\begin{smallmatrix}\diagup H\\ -NH_2\\ \diagdown NH_2\end{smallmatrix} & -NH_3 = & -C\begin{smallmatrix}\diagup H\\ =NH\end{smallmatrix} \\ =C<\begin{smallmatrix}NH_2\\ NH_2\end{smallmatrix} & -NH_3 = & =C=NH \end{array}$$

These two imides correspond to the aldoximes and ketoximes respectively.

Of the triamides, in which the three amido groups are connected with the same carbon atom, but one is derivable, *viz.*, that from the methyl group, which is the only simple hydrocarbon group containing the requisite number of hydrogen atoms. By splitting off ammonia it may yield first the amidine, and then the nitrile, as indicated by the following formulas:



$$\underbrace{-C\begin{array}{l}\diagup NH_2\\ -NH_2\\ \diagdown NH_2\end{array}}_{\text{Triamide}} \quad -NH_3 = \quad \underbrace{-C\begin{array}{l}\diagup NH_2\\ \diagdown\!\!\diagdown NH\end{array}}_{\text{Amidine}}$$

$$\underbrace{-C\begin{array}{l}\diagup NH_2\\ \diagdown\!\!\diagdown NH\end{array}}_{\text{Amidine}} \quad -NH_3 = \quad \underbrace{-C\equiv N}_{\text{Nitrile}}$$

In the following table the simple types, ten in all, of the amido substitution products and their deammoniated compounds are given:

Hydrocarbon Groups	Monamides	Diamides		Triamides		
$-C\begin{array}{l}\diagup H\\ -H\\ \diagdown H\end{array}$	$-C\begin{array}{l}\diagup NH_2\\ -H\\ \diagdown H\end{array}$	$-C\begin{array}{l}\diagup NH_2\\ -NH_2\\ \diagdown H\end{array}$		$-C\begin{array}{l}\diagup NH_2\\ -NH_2\\ \diagdown NH_2\end{array}$		
			$-C\begin{array}{l}\diagup\!\!\diagup NH\\ \diagdown H\end{array}$		$-C\begin{array}{l}\diagup\!\!\diagup NH\\ \diagdown NH_2\end{array}$	
						$-C\equiv N$
$=C\begin{array}{l}\diagup H\\ \diagdown H\end{array}$	$=C\begin{array}{l}\diagup NH_2\\ \diagdown H\end{array}$	$=C\begin{array}{l}\diagup NH_2\\ \diagdown NH_2\end{array}$				
			$=C=NH$			
$\equiv CH$	$\equiv CNH_2$					

The possibility of splitting off ammonia in a different manner will not be discussed at this point.

OTHER SUBSTITUTION PRODUCTS

With the halogen substitution products, we have disposed, with the exception of manganese, of the known elements of the seventh group of the periodic system, *i. e.*, so far as the simple elemental substitution products are concerned. These constitute by far the bulk of halogen organic compounds.

Like the oxygen derivatives, so the sulphur, selenium, and tellurium derivatives can be derived by the substitution of their simple hydride groups for hydrogen, and the subsequent splitting off of sulphuretted hydrogen, etc. Such compounds as sulphates, sulphites etc., are easily derived as are the corresponding derivatives of the organic acids.

Analogous to the amides are the phosphines, arsines etc. What has been said of the sulphates applies also to phosphates, arsenates, etc.

We now arrive at the fourth group of the periodic system. The typical organic element of this group is carbon. Its simplest univalent hydride group is the methyl group. By the substitution of this methyl group for a hydrocarbon hydrogen we obtain a homologue of the hydrocarbon in question. This brings us back to the hydrocarbons.

The classification of substitution products obtained by the substitution of elements of groups three, two, one, and eight, need not concern us at present.

Genetic Relationship Of Types

We have thus far reduced the large bulk of simple carbon compounds to relatively few types. While it should always be remembered that the properties of a compound are functions of its structure, and that the structure of a compound implies more than the peculiar characteristics of the type or types to which it belongs, yet the type is of fundamental importance. It is essentially the same irrespective of degree of saturation, of chain or cyclic character, and of the number of carbon atoms. Differences are primarily differences of degree. All of these factors, however, exert a modifying influence, as does also the piling up of a number of the same type groups within the same molecule.

These are matters to be brought out later, at least in so far as they exert an influence on the mode of classification. For the present, however, we are concerned with simple types only.

The advantages of the system of classification thus far outlined are those of simple logical questions and answers, based on a definition that foreshadows the questions. Organic chemistry being defined as the chemistry of the hydrocarbons and their substitution products, the latter are naturally classified into mono-, di-, tri-, etc. substitution products, that is, according to the number of times substitution has taken place, irrespective of the substituting element or radicle. Taking into consideration that there are three simple hydrocarbon groups of which all hydrocarbons are made up, it follows that there must be three types of mono-substitution products. For the same reason there are two types of di-substitution products, and but one of tri-substitution products in which substitution has taken place in connection with the same carbon atom. If substitution takes place in connection with different carbon atoms, no new simple types, as has already been pointed out, are formed.

A system of classification based on rational questions and answers would certainly be a gain over a mode of classification based on several historical systems. While different points of view are not only an advantage, but a necessity, in the study of chemistry, in the classification of compounds a unitarian point of view should be maintained if possible.

But even such a gain might not be worth the trouble involved in a change if the system proposed did nothing more than to effect a systematic pigeonholing of chemical compounds. A rational classification based on chemical structure, and on the theory that the properties of a chemical compound are functions of its structure, must accomplish much more. It must bring out the genetic relationship of the different types.

This genetic relationship can be brought out in several ways. Suffice it for the present to bring out the relationship between the simple underlying hydrocarbon groups and the types of the three classes of mono-, di-, and tri-valent elements utilized thus far for purposes of illustration. This relation can best be revealed with the aid of tabulated structural formulas.

Types of Mono-substitution Products

Hydrocarbon groups	Halides	Hydroxides	Amides
$-CH_3$	$-CH_2X$	$-CH_2OH$	$-CH_2NH_2$
$=CH_2$	$=CHX$	$=CHOH$	$=CHNH_2$
$\equiv CH$	$\equiv CX$	$\equiv COH$	$\equiv CNH_2$

Adopting a style of nomenclature that was originally, so far as the compounds here involved are concerned, applied to the hydroxides or alcohols, we distinguish the three types by designating them primary, secondary, and tertiary, respectively. For a long time this mode of distinction has also been applied to the corresponding halides, but not to the corresponding amides. It is right here that the irrationality of mixing systems of classification and nomenclature is keenly felt. For our purposes we shall, therefore, adhere rigidly to what appears to be the only rational solution of this confused condition. A primary mono-substitution product is a compound in which this substitution has taken place in connection with a methyl group of a hydrocarbon. A secondary compound, one in which the substitution has taken place in connection with a methylene group, and a tertiary compound, one in which it has taken place in connection with a methenyl group. Or in other words, using the structural groups tabulated above, a primary alcohol is a compound characterized by a $-CH_2OH$ group; a secondary halide, a compound characterized by a $=CHX$ group, a tertiary amide a compound characterized by a $\equiv CNH_2$ group.

If it be continually borne in mind that these group formulas, like the complete formulas of chemical compounds, are but the chemical shorthand for the properties involved, no harm can result. It may not be amiss, therefore, to review a few of these properties, well known as they are. Using the most general expressions, they can be represented by the equations:

$$\begin{array}{llll} R'H + X_2 & = R'X & + HX \\ R'X + M'OH & = R'OH & + M'X \\ R'X + HNH_2 & = R'NH_2 & + HX \end{array}$$

Thus it is possible to pass by simple reactions from the hydrocarbon to the halide, and from the halide to the hydroxide and amide. It is also possible to reverse the order *e. g.,* from the hydroxide to the halide:

$$R'OH + HX = R'X + H_2O;$$

or from the amide, through the di-azo compound, to either the alcohol

$$R'NH_2 + ONOH = R'N{=}NOH + H_2O$$
$$R'N{=}NOH = R'OH + N_2;$$

or by first converting the diazo compound into diazo-halide, to the simple halide

$$R'N{=}NX = R'X + N_2.$$

Finally it is possible, by so-called inverse substitution, to reduce the halide to the hydrocarbon:

$$R'X + XH = R'H + X_2.$$

Thus the cycle of changes is completed.

By using the partly analyzed formulas as indicated by the type formulas tabulated above, it becomes apparent how a primary halide will yield a primary alcohol, or a tertiary amide upon diazotation, a tertiary alcohol, etc. A host of organic reactions can thus be grouped into a few type reactions which follow from the method of classification. When such results are possible, the mere pigeonholing certainly can be regarded as a mere incident, though practically an important one, in a system of classification and nomenclature.

TYPES OF DI-SUBSTITUTION PRODUCTS

Hydrocarbon groups	Halides	Hydroxides		Amides	
$-C\begin{array}{l}\diagup H\\ -H\\ \diagdown H\end{array}$	$-C\begin{array}{l}\diagup H\\ -X\\ \diagdown X\end{array}$	$-C\begin{array}{l}\diagup H\\ -OH\\ \diagdown OH\end{array}$		$-C\begin{array}{l}\diagup H\\ -NH_2\\ \diagdown NH_2\end{array}$	
			$-C\begin{array}{l}\diagup H\\ \diagdown\!\!\diagdown O\end{array}$		$-C\begin{array}{l}\diagup H\\ \diagdown\!\!\diagdown NH\end{array}$
$=C\begin{array}{l}\diagup H\\ \diagdown H\end{array}$	$=C\begin{array}{l}\diagup X\\ \diagdown X\end{array}$	$=C\begin{array}{l}\diagup OH\\ \diagdown OH\end{array}$		$=C\begin{array}{l}\diagup NH_2\\ \diagdown NH_2\end{array}$	
			$=C=O$		$=C=NH$
$\equiv CH$					

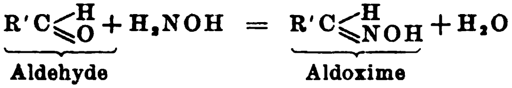
Here again genetic relationship becomes apparent as expressed by such well-known reactions as the following:

$$R'CHX_2 + 2M'OH = R'CHO + H_2O + 2M'X$$
$$R'_2CX_2 + 2M'OH = R'_2CO + H_2O + 2M'X$$

As is well known these reactions also are reversible:

$$R'CHO + X_2PX_3 = R'CHX_2 + OPX_3$$
$$R'_2CO + X_2PX_3 = R'_2CX_2 + OPX_3$$

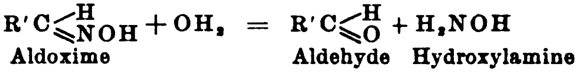
If in place of the imides, resulting upon deammoniation from the diamides, we substitute their hydroxy or oxy derivatives, the oximes, the genetic relationship between aldehydes and ketones, on the one hand, and their respective oximes, on the other hand, is readily expressed by the following general equations:



$$\underbrace{R'C\begin{smallmatrix}H\\O\end{smallmatrix}}_{\text{Aldehyde}} + H_2NOH = \underbrace{R'C\begin{smallmatrix}H\\NOH\end{smallmatrix}}_{\text{Aldoxime}} + H_2O$$

$$\underbrace{R_2'C = O}_{\text{Ketone}} + H_2NOH = \underbrace{R'_2C = NOH}_{\text{Ketoxime}} + H_2O$$

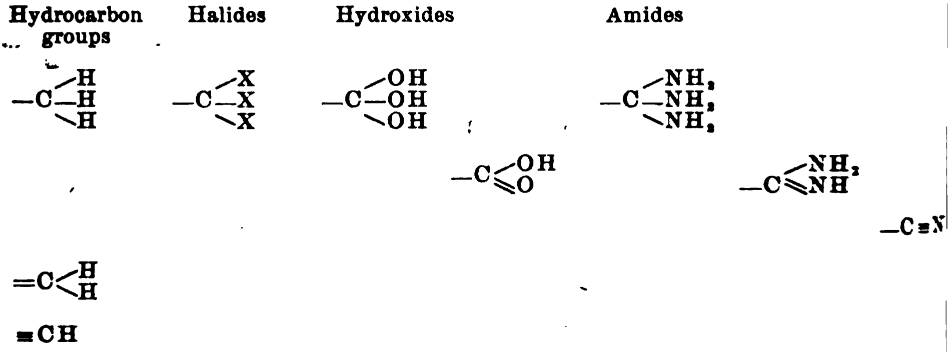
Whereas the oximes result upon condensation, upon hydrolysis they may be caused to resolve into their components, hydroxylamine and either aldehyde or ketone.



$$\underset{\text{Aldoxime}}{R'C\begin{smallmatrix}H\\NOH\end{smallmatrix}} + OH_2 = \underset{\text{Aldehyde}}{R'C\begin{smallmatrix}H\\O\end{smallmatrix}} + \underset{\text{Hydroxylamine}}{H_2NOH}$$

$$\underset{\text{Ketoxime}}{R'_2C{=}NOH} + OH_2 = \underset{\text{Ketone}}{R'_2C{=}O} + \underset{\text{Hydroxylamine}}{H_2NOH}$$

TYPES OF TRI SUBSTITUTION PRODUCTS



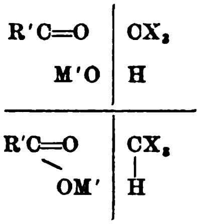
Hydrocarbon groups	Halides	Hydroxides		Amides	
$-C\begin{smallmatrix}H\\H\\H\end{smallmatrix}$	$-C\begin{smallmatrix}X\\X\\X\end{smallmatrix}$	$-C\begin{smallmatrix}OH\\OH\\OH\end{smallmatrix}$		$-C\begin{smallmatrix}NH_2\\NH_2\\NH_2\end{smallmatrix}$	
			$-C\begin{smallmatrix}OH\\O\end{smallmatrix}$		$-C\begin{smallmatrix}NH_2\\NH\end{smallmatrix}$
					$-C\equiv N$
$=C\begin{smallmatrix}H\\H\end{smallmatrix}$					
$\equiv CH$					

A number of well-known reactions might be cited to point out the genetic relationship indicated by the above group formulas. A few may suffice.

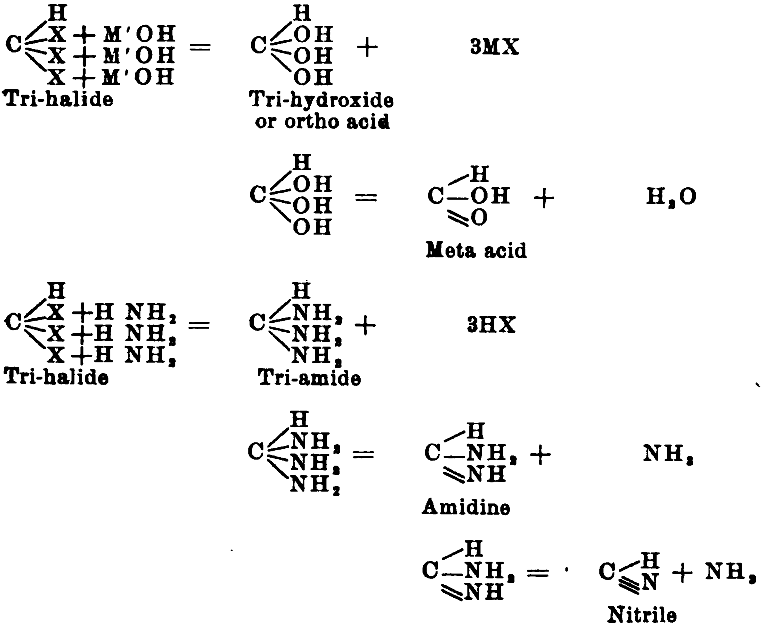
Under certain conditions all three hydrogen atoms of a methyl group can be replaced readily by halogen:

$$R'COCH_3 + X_6 = R'COCX_3 + 3HX.$$

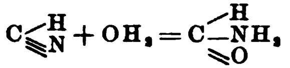
The above tri-halide is readily hydrolized to methenyl or formyl tri-halide (chloroform, bromoform and iodoform).



The tri-halide thus resulting can be converted either into the tri-hydroxide or ortho acid and its dehydration product, the meta acid, or through the triamide into the corresponding amidine and nitrile.

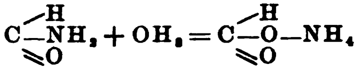


The nitrile in turn can be hydrolized to the acid through the acid amide:



$$C\left\langle\begin{matrix}H\\ \equiv N\end{matrix}\right. + OH_2 = C\left\langle\begin{matrix}H\\ NH_2\\ =O\end{matrix}\right.$$

Nitrile Acidamide



$$C\left\langle\begin{matrix}H\\ NH_2\\ =O\end{matrix}\right. + OH_2 = C\left\langle\begin{matrix}H\\ O-NH_4\\ =O\end{matrix}\right.$$

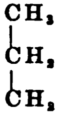
Ammonium salt of acid

Other genetic relationships, as *e. g.*, between mono-, di-, and tri-, substitution products, can be brought out. Thus the student in organic chemistry is taught that the difference between a primary, secondary and tertiary alcohol consists in this, that the primary alcohol can readily be oxidized to an aldehyde and an acid with the same number of carbon atoms, the secondary alcohol to a ketone, and that the tertiary alcohol is not capable of similar oxidation. This fact was first emphasized by Kolbe basing his structural notions on the type carbinol. Having abandoned the theory of types to a large extent, the above definitions have largely lost their structural significance, at least as brought out in textbooks. The structural significance is again emphasized, but from the unitarian point of view of our definition of organic chemistry, *viz.*, that organic chemistry is the chemistry of the hydrocarbons and their substitution products.

MULTIPLICATION OF TYPES

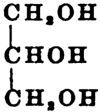
Thus far only those substitution products have been considered in which substitution has taken place in connection with the same carbon atom. It has already been pointed out that substitution in connection with different carbon atoms produces no new types but merely a multiplication of types already developed. This becomes apparent if we but recall that with the exception of methane all hydrocarbons are composed, so far as substitution is concerned, of the three simple groups used in developing types thus far studied. This *a priori* reasoning is in accord with the facts. A few relatively simple and well-known illustrations will clearly reveal this.

Thus, *e. g.*, glycerin is a tri-atomic alcohol in which the three hydroxy groups are associated one with each of the three carbon atoms as represented by the following formula referable to propane.



$$\begin{array}{l} CH_3 \\ | \\ CH_2 \\ | \\ CH_3 \end{array}$$

Propane

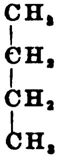


$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

Propane-triol—1, 2, 3, or glycerin.

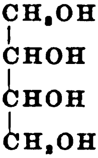
It is twice a primary alcohol and once a secondary alcohol and the above chemical shorthand expression is in accordance with the properties of this substance.

Erythrol is a similar tetratomic alcohol and some of its properties find expression in the formula of tartaric acid to which it can be oxidized.



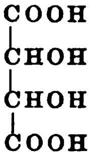
$$\begin{array}{l} CH_3 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ CH_3 \end{array}$$

Butane



$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

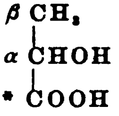
Erythrol



$$\begin{array}{l} COOH \\ | \\ CHOH \\ | \\ CHOH \\ | \\ COOH \end{array}$$

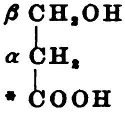
Tartaric acid

With the multiplication of types, it becomes necessary to indicate their position. This is done in a variety of ways. Thus the letters of the Greek alphabet have been used.



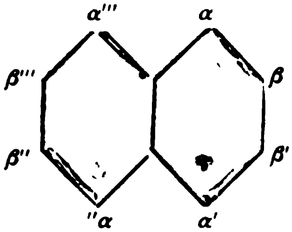
$$\begin{array}{l}\beta\ CH_3\\ \quad|\\ \alpha\ CHOH\\ \quad|\\ *\ COOH\end{array}$$

α—Lactic acid

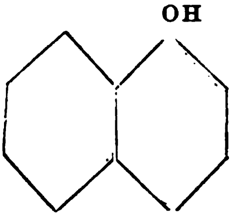


$$\begin{array}{l}\beta\ CH_2OH\\ \quad|\\ \alpha\ CH_2\\ \quad|\\ *\ COOH\end{array}$$

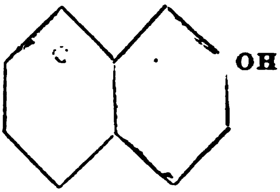
β—Lactic acid



Naphthalene

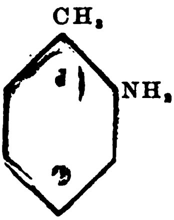


α—Naphthol

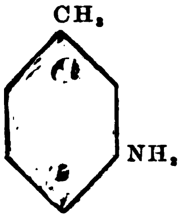


β—Naphthol

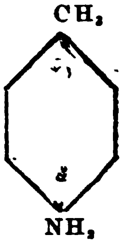
Abbreviations for neighboring (o = ortho), opposite (p = para), and intermediate (m = meta) were suggested by Kekulé to indicate the positions in connection with di-substitution products of benzene.



o—Toluidine

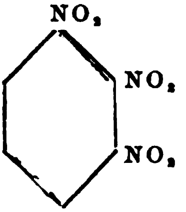


m—Toluidine

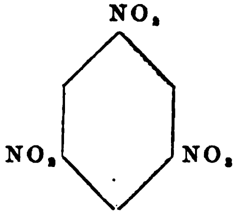


p—Toluidine

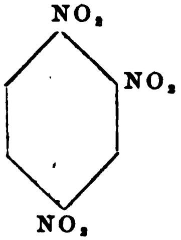
In connection with the tri-substitution products of benzene, the abbreviations for neighboring (v) = vicinal, (s) = symmetric, and (a) = asymmetric were likewise suggested by Kekulé.



v—Trinitro benzene



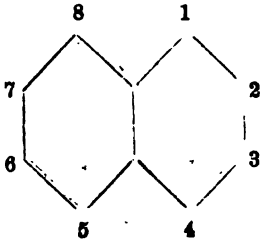
s—Trinitro benzene



a—Trinitro benzene

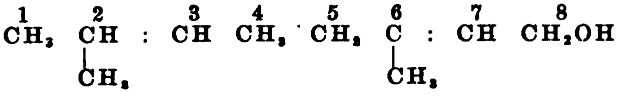
For more special purposes, special symbols have been suggested, as, *e. g.*, N for "Nor" derivatives of heterocyclic compounds, etc.

Numbers have also been used and are being used more and more. Thus the ten isomeric di-substitution products of naphthalene have long been indicated by numbers.



The Geneva Congress* suggested the exclusive use of numbers and no doubt, thereby prepared the way for a simpler nomenclature. Not only are numbers used to indicate the position of type groups, but of double bonds, the structural equivalents of hydrogen as well.

The application of these rules to recent structural research may best be illustrated with the aid of a few formulas.



$$\overset{1}{CH_3}\ \underset{\overset{|}{CH_3}}{\overset{2}{CH}}\ :\ \overset{3}{CH}\ \overset{4}{CH_2}\cdot\overset{5}{CH_2}\ \underset{\overset{|}{CH_3}}{\overset{6}{C}}\ :\ \overset{7}{CH}\ \overset{8}{CH_2OH}$$

Di-methyl-2, 6- octa-diene-2, 6-ol- 8; or geraniol

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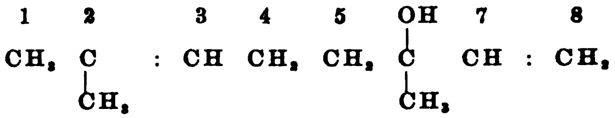
* See Tiemann's account of the Congress in Ber. d. d. chem. Ges., 26, p. 1595. An abridged account can be found in Richter-Anschuetz-Smith, *Organic Chemistry*, 3rd Am. ed. (1899), vol. 1, p. 57.



$$\overset{1}{CH_3}\ \underset{CH_3}{\overset{2}{C}}\ :\ \overset{3}{CH}\ \overset{4}{CH_2}\ \overset{5}{CH_2}\ \underset{CH_3}{\overset{OH}{C}}\ \overset{7}{CH}\ :\ \overset{8}{CH_2}$$

Dimethyl-2, 6- octadiene- 2, 7- ol-6; or linalool

The nomenclature of organic chemistry naturally reflects basal theories and these again underlie classification. Hence rational nomenclature and classification go hand in hand. While the Geneva Congress paved the way, in part, for a more rational naming of carbon compounds, it could not get very far, because it had no rational classification as a necessary basis for its deliberations and rules. Hence it did not get beyond propositions for the nomenclature of chain compounds.

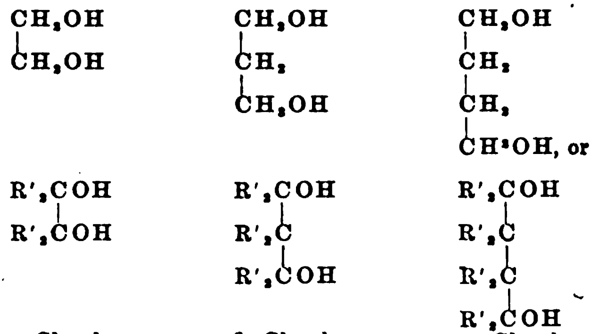
HETEROCYCLIC COMPOUNDS

Practically all carbocyclic compounds are readily taken care of when referred to the underlying carbocyclic hydrocarbons. How these can be classified has already been pointed out. Difficulty has arisen, however, in the classification of heterocyclic compounds. The conventional classification, or rather lack of classification, of these compounds is one of the serious drawbacks of our text and reference works on organic chemistry.

The most important of these are again those oxygen and nitrogen compounds containing one or more oxygen or nitrogen atoms in the cycle or ring. But it is a comparatively easy matter to classify them along rational lines, both of chemical structure and genetic relationship. As before, the oxygen compounds will be taken up first.

It has already been pointed out that hydroxy substitution in connection with different carbon atoms of the underlying hydrocarbons does not produce new types. This statement is true only in so far as the hydroxy substitution products themselves are concerned. This point has been illustrated by a few well-known formulas. It has also been pointed out that in such compounds the position of the substituting groups plays a more or less important role and should be considered in connection with the classification of these compounds.

Thus, *e. g.*, those glycols in which the two hydroxy groups are connected with different carbon atoms may be subclassified into alpha, beta, gamma etc., glycols. Series of such glycols may be represented either by their initial members or by type formulas.



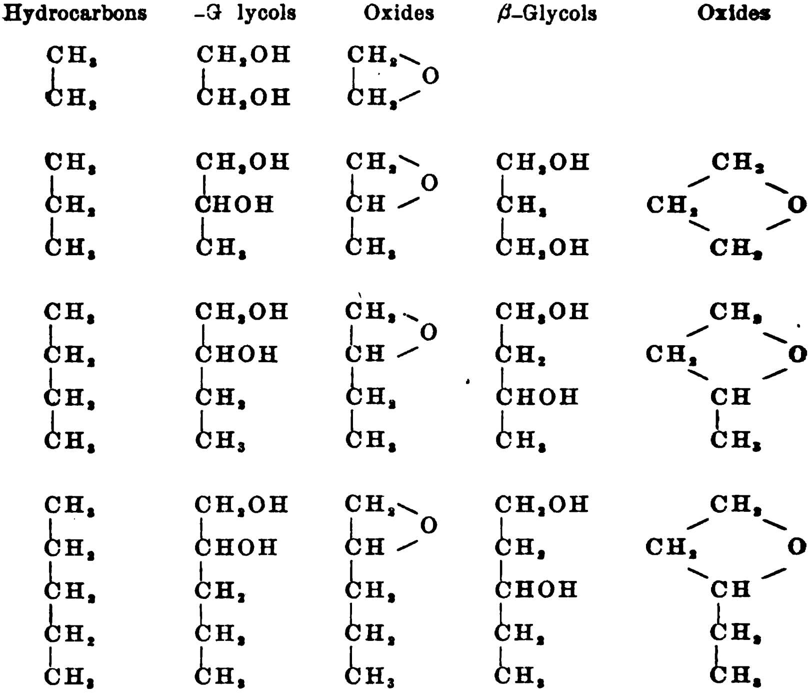
$$\begin{array}{lll} CH_2OH & CH_2OH & CH_2OH \\ | & | & | \\ CH_2OH & CH_2 & CH_2 \\ & | & | \\ & CH_2OH & CH_2 \\ & & | \\ & & CH^{2}OH\text{, or} \end{array}$$

$$\begin{array}{lll} R'_2COH & R'_2COH & R'_2COH \\ \quad | & \quad | & \quad | \\ R'_2COH & R'_2C & R'_2C \\ & \quad | & \quad | \\ & R'_2COH & R'_2C \\ & & \quad | \\ & & R'_2COH \end{array}$$

α—Glycols β—Glycols γ—Glycols

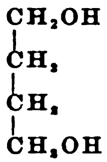
Whereas those glycols which contain both hydroxy groups connected with the same carbon atom, as a rule, split off water very readily, thereby yielding aldehydes and ketones respectively; those glycols in which the two hydroxy groups are connected with different carbon atoms split off the elements of water much more reluctantly. Moreover, the ease with which they split off water depends upon the position of the hydroxy groups. Thus, gamma, delta and epsilon glycols yield a molecule of water from the two hydroxy groups much more readily than do the alpha and beta glycols, for the reason that rings with five, six and seven members, are, as a rule, much more stable than those with three and four members.

The classification of these glycols and their corresponding oxides can best be demonstrated in two ways: first by their derivation from the underlying hydrocarbons, and secondly by the development of homologous series from the types thus established.

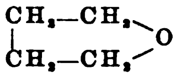


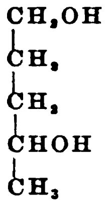
In the above table only those glycols and their corresponding oxides derivable from normal hydrocarbons have been recorded simply as a matter of convenience. Having established the types of glycols and oxides, it is an easy matter to take the first member of each series and use it as the starting point for the development of an homologous series.

γ-Glycols **Oxides** **δ-Glycols** **Oxides**

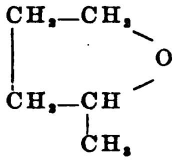


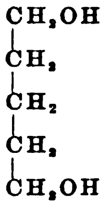
$$\begin{array}{l}CH_2OH\\ |\\ CH_2\\ |\\ CH_2\\ |\\ CH_2OH\end{array}$$



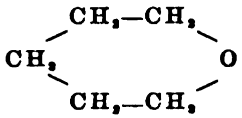


$$\begin{array}{l}CH_2OH\\ |\\ CH_2\\ |\\ CH_2\\ |\\ CHOH\\ |\\ CH_3\end{array}$$

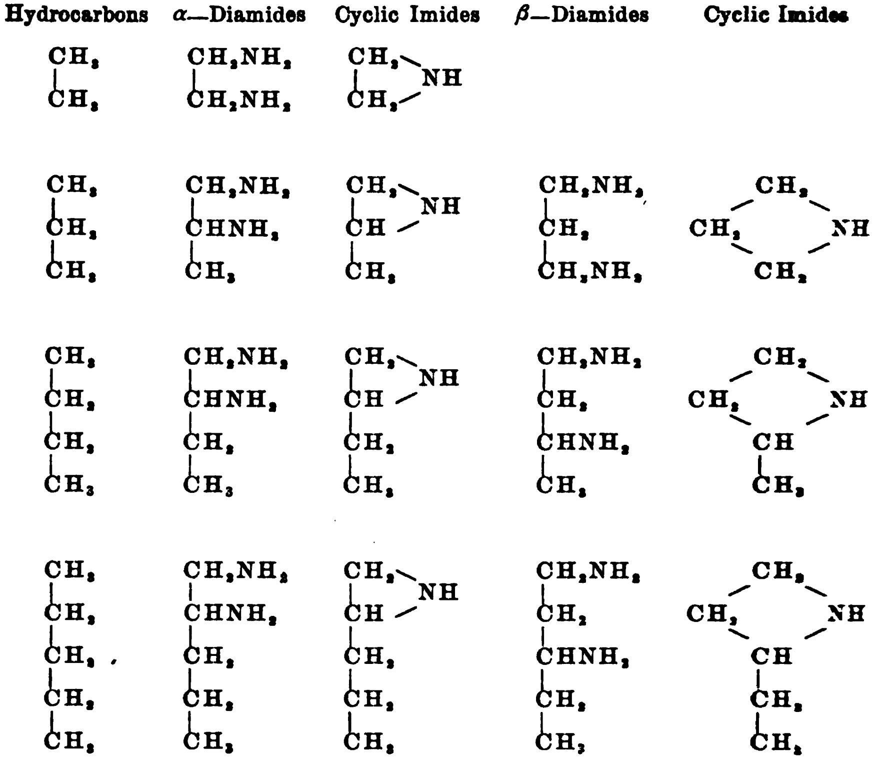




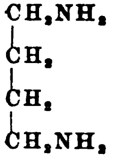
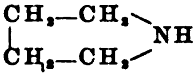
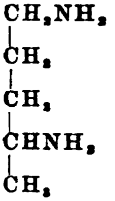
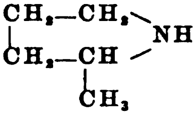
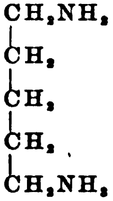
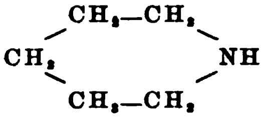
$$\begin{array}{l}CH_2OH\\ |\\ CH_2\\ |\\ CH_2\\ |\\ CH_2\\ |\\ CH_2OH\end{array}$$



In a similar manner heterocyclic compounds with two oxygen atoms to the cycle can be referred to and derived from the glycols. Both the simple oxides (dimethylene oxide, trimethylene oxide, etc.) as well as the heterocyclic compounds with two oxygen atoms should be subordinated, for purposes of classification, to the glycols, as the monoxygen ethers are to the monatomic alcohols.



The same principle of classification applies to the heterocyclic compounds with one or more nitrogen atoms in the ring. Those with one nitrogen atom can be derived from the corresponding diamines by deammoniation as the oxides were derived from the

—γDiamides	Cyclic Imides	δ—Diamides	Cyclic Imides
			
			

glycols by dehydration. Like the alkyl derivatives of the monamines, these cyclic imines should be subordinated, for purposes of classification, to the corresponding diamines. The types of cyclic imines referable to diamines of the limit series are tabulated above.

APPENDIX A

ARRANGEMENT ACCORDING TO THE NUMBER OF CARBON ATOMS

The arrangement of carbon compounds according to the number of carbon atoms or equivalents became possible only after a large number of organic compounds had been analyzed. In a way it may be regarded as the basal empirical classification, the importance of which might easily be overestimated when quantitativeness was a dominant thought in chemistry. Strange as it may now seem, it does not appear that such an arrangement was seriously suggested immediately, even after Liebig had perfected the technique of organic analysis, thus making possible the determination of carbon atoms or carbon equivalents, much less shortly after the idea of quantitativeness became the dominant idea in chemistry with the antiphlogistic theories of Lavoisier. It is rather significant that such an arrangement of organic compounds was carried out in all seriousness in one of the principal hand books of chemistry only after the dogmatism of the first half of the nineteenth century had caused the partial shipwreck of organic theories.

The primary classification of carbon compounds according to the number of carbon atoms was put into practice in Lepold Gmelin's comprehensive and extensively used *Handbuch der Chemie,* the first edition of which had appeared in 1817, and which is best known to English speaking chemists through Watt's translation published by the Cavendish Society.

A conspicuous example of a modern text, or rather handbook, of chemistry in which the same primary classification occurs is the well known *Treatise on Chemistry* by Roscoe and Schorlemmer, volume three of which, the first part of organic chemistry, appeared in 1890.

APPENDIX B

CLASSIFICATION AS REVEALED BY TABLES OF CONTENTS.

One of the earliest texts on chemistry devoid of alchemistic jargon is that of Lemery, the first edition of which appeared in 1675. It not only appeared in numerous editions during his life time, but its publication was continued long after the author's death. Moreover, it was translated into English, Dutch, German and Italian. For more than a century it exerted a decided influence on chemical thought. Like most books of historical interest, Lemery's *Cours de Chymie* is not generally available. For this reason, a small part of the table of contents (edition of 1756) is herewith reproduced:

LEMERY, *Cours de Chymie*

Des Minéraux
- I. De l'or.
- II. De l'argent, etc.

Des Végétaux
- I. Du jalap, résine ou magistere du jalap.
- II. De la rhubarbe, extrait de rhubarbe.
- V. De la canelle, huile ou essence de canelle, son eau étherée, tincture de canelle.
- XIX. Du sucre, esprit de sucre.
- XXI. Du vinaigre, distillation du vinaigre.
- XX. Du vin, distillation de vin et eau-de-vie, esprit de vin, etc.
- XXII. Du tartre, crystal de tartre, tartre soluble ou sel vegetal, crystal du tartre chalybé ou martial, tartre martial soluble, tartre emetique, etc.
- XXXII. Du camphre.

Des Animaux
- I. De la vipre, destillation de la vipre.
- V. Du miel, etc.
- VI. De la cire, etc.

The very limited scope of the organic materia chemia at the close of the 18th century becomes apparent from the following table of contents, viz. that of

F. A. C. Gren: *Grundriss der Naturlehre in seinem mathematischen und chemischen Theile neu bearbeitet.* 1793.

Bestandtheile der Koerper der drey Naturreiche. (p. 255).

Mineralische Substanzen (p. 256): Die Koerper des Mineralreiches, oder die unorganischen Koerper lassen sich fueglich in fuenf Classen abtheilen, nemlich Salze, Erden, Metalle, Erdharze, und Schwefel.

Bestandtheile der Pflanzenkoerper (p. 318): Zu den naeheren Bestandtheilen des Pflanzenreiches rechne ich:

1.) Schleim oder Gummi
2.) Harz
3.) Kleber
4.) Staerkeartigen Theil
5.) Zucker
6.) Weinsteinsaeure
7.) Sauerkleesalzsaeure
9.) Aepfelsaeure
10.) Essigsaeure
11.) Benzoesaeure
12.) Zusammenziehenden Stoff
13.) Fettes Oel
14.) Aetherisches Oel
15.) Kampher
16.) Scharfen Stoff und
17.) Narcotischen Stoff.

Bestandtheile der thierischen Koerper (p. 344): Als naehere Bestandtheile des thierischen Koerpers sind bekannt:

1.) Gallerte
2.) Fett
3.) Lymphe
4.) Fadenartiger Theil
5.) Knochenmaterie und
6.) Milchzucker
7.) Ameisensaeure und
8.) Das scharfe Harz der spanischen Fliegen.

Practically the same list of "naeheren Bestandtheilen, die als solche in Koerpern des Gewaechsreiches praeexistiren" is enumerated in Gren's *Systematisches Handbuch der gesamten Chemie* of 1794 (vol. 2. p. 3.)

That the number of organic substances had grown but little shortly after Lavoisier's death becomes apparent from the following list. Though Lavoisier's point of view is primarily that of oxygen and combustion the distinction between vegetable and animal acids is clearly marked.

A. Lavoisier: *Traité élémentaire de chimie.* 1801.

Lavoisier's point of view is that of oxygen: oxydation and combustion. Having considered the four simple combustible substances, viz., phosphorus, sulphur, carbon, and hydrogen, he turns to the combustion of vegetable fats. This leads him to the consideration of "the composition of vegetable and animal substances" in general (I. p. 123). Those substances related to carbonic acid, the product of combustion, are naturally of prime interest to him. He names them, in accordance with his system of nomenclature of mineral acids, as follows:

Vegetable

L'acide acéteux
L'acide acétique
L'acide oxalique
L'acide tartareux
L'acide pyro-tartareux
L'acide citrique
L'acide malique
L'acide pyro-muquex
L'acide pyro-ligneux
L'acide gallique
L'acide benzoïque
L'acide camphorique
L'acide succinique

Animal

L'acide lactique
L'acide saccho-lactique
L'acide bombique
L'acide formique
L'acide sébacique
L'acide prussique

The same point of view naturally leads him to take up next the products of destructive distillation (I, p. 132) of vegetable and animal substances, among which he mentions Dippel's oil.

Inasmuch as carbonic acid is one of the principal products of the fermentation of saccharine liquids, the process of vinous fermentation comes next (p. 139) to be followed by putrid fermentation (p. 153) and acetous fermentation (p. 159).

The consideration of acids is followed by that of the salts, the organic (pp. 277–322) following the inorganic (pp. 231–276).

A more compendious list is enumerated in the ten volume works of

A. F. Fourcroy: *Système des connaissances chimiques.* 1800. On vegetable organic compounds (Volume 7).

1. Juice
2. Mucous, mucilage and gums
3. Sugar
4. Vegetable acids
    - A. "Acides natifs et purs."
        - a) Gallic acid
        - b) Benzoic acid
        - c) Succinic acid
        - d) Malic acid
        - e) Citric acid
    - B. "Acidules"
        - a) Oxalic acid
        - b) Tartarous acid
    - C. "Acides empyreumatiques."
        - a) Pyromucous acid
        - b) Pyrotartarous acid
        - c) Pyroligneous acid
    - D. Acids not found as such in nature
        - a) Mucous acid
        - b) Camphoric acid
        - c) Suberic acid
    - E. Artificial acids corresponding to natural acids
        - a) Malic acid
        - b) Tartarous acid
        - c) Oxalic acid
    - F. Acids produced by fermentation
        - a) Acetous acid
        - b) Acetic acid
5. Farinaceous substance
6. Gluten
7. Extractive
8. Fixed oil

9. Fat and wax
10. Volatile oil
11. Camphor
12. Resins
13. Gum-resins
14. Caoutchouc
15. Balsams
16. Pigments
17. Vegetable albumen
18. Woody substance
19. Tannin
20. Cork
21. Fossil and mineral substances

This classification according to the three natural kingdoms with the sub-classification of phytochemistry and zoochemistry not only extended to the systems of Berzelius and Liebig, but still finds its way into the lumber chambers of unclassified compounds of modern organic chemistries.* That it should have constituted the fundamental classification of phytochemistry as late as the seventies of the last century is, therefore, not surprising. The same conservatism went one step farther when pharmaceutical authors dignified this abandoned chemical point of view by calling it a "pharmaceutical" classification of chemicals.

To what extent organic chemistry was the chemistry of plant constituents even in 1837 becomes apparent from the following partial table of contents taken from Woehler's translation of Berzelius' *Lehrbuch der Chemie.*

NAEHERE BESTANDTHEILE PFLANZEN

I. Klasse: Pflanzensaeuren (with thirty-three titles).
II. Klasse: Vegetablische Salzbasen (with twenty-two titles).
III. Klasse: Indifferente Pflanzentoffe.
    1. Staerke
    2. Gummi und Pflanzenschleim
        a. Gummi
        b. Pflanzenschleim

---

* e. g. Richter-Anschuetz-Smith, vol. 2, pp. 384 et seq.

- 3. Zucker
    - a. Rohrzucker
    - b. Traubenzucker
    - c. Mannazucker
    - d. Schwammzucker
    - e. Suessholzzucker
- 4. Pflanzenleim und Pflanzeneiweiss
- 5. Pectin und Pectinsaeure
- 6. Pollenin
- 7. Fette Oele
    - (c) Trockende Oele
    - (2) Nicht " "
    - (3) Feste Oele

Seifenbildungsprocess und seine Producte

- a. Eigentliche fette Saeuren, d. h. solche, welche bei der Destillation mit Wasser nicht mit uebergehen
- b. Durch den Seifenbildungsprocess erzeugte fluechtige Saeuren
- c. Glycerin oder Oelzucker
- d. Seife

Einfluss der Saeuren bei der Zersetzung der Oele

Fluechtige Oele

- a. Sauerstofffreie fluechtige Oele
- b. Sauerstoffhaltige " "
    - a) Aromatische Oele
    - b) Scharfe und blasenziehende Oele
    - c) Blausaeurehaltige giftige Oele
    - d) Campher

Harze

Extracte und extractfoermige Stoffe

- A. Rothe Pflanzenfarben
- B. Gelbe "
- C. Gruene "
- D. Blaue "

Skelett der Pflanzen

- a. Mark
- b. Holz und Pflanzenfaser
- c. Rinde

Von den fett-und harzhaltigen Milchsaeften der Pflanzen und den sogenannten Gummiharzen

Wurzeln
Rinden
Holzarten
Kraeuter und Schwaemme
Blaetter
Bluethen
Fruechte und Samen

APPENDIX C

DEFINITIONS OF ORGANIC CHEMISTRY

Gmelin. "The bodies of the organic kingdom are distinguished, in their most complete state, from those of the inorganic kingdom:

1. By their inherent vital force.
2. By a peculiar structure, internal and external.
3. By being composed, for the principal and most important part at least, of chemical compounds quite peculiar to them, called Organic compounds, or Proximate principles of the organic kingdom, which occur in the bodies of plants and animals, partly mixed and partly combined, both with one another and with certain inorganic compounds."

"The proximate principles into which an organic body may be resolved, either by mechanical or by chemical means, are partly inorganic, such as water, carbonic acid, and other mineral acids; partly organic. When the latter are of such a nature, that any attempt to decompose them further leads to the formation of decomposition products, which when reunited, produce something totally different from the substance originally decomposed, they are regarded as Primary, or Elementary Organic Compounds."

Handbook of Chemistry. Translation of the 4th edition. Vol. 7, p. 1.

Gerhardt. "Die organische Chemie hat die Aufgabe, die Koerper, welche durch die Verbindung dieser Elemente (namely carbon, hydrogen, nitrogen and oxygen, and occasionally sulphur, phosphorus, metals, etc.) entstehen, zu untersuchen, und zwar in Beziehung auf ihre Eigenschaften, ihre Zusammensetzung und auf die Gesetze, nách welchen ihre Verwandlungen erfolgen. Da alle organischen Verbindungen ohne Ausnahme Kohlenstoff enthalten, so koennte man die organische Chemie die Chemie

des Kohlenstoffs nennen. Sie betrachtet die organischen Substanzen nur in ihren rein chemischen Beziehungen, ohne Ruecksicht auf ihre Rolle im Organismus . . ."

"Alle Gebilde, Secretionen und Organe des Pflanzen-und Thierkoerpers sind Mischungen von organischen Stoffen in verschiedenen Verhaeltnissen. Die organische Chemie gibt die Mittel an, diese bestimmten Bestandtheile, deren Zusammensetzung unter denselben Umstaenden genau dieselbe und unveraenderlich ist, von einander zu trennen und sie in dem Zustande der Reinheit darzustellen. Sie allein gehoeren ins Gebiet der organischen Chemie."

Grundriss de organischen Chemie. Aus dem Franzoesischen uebersetzt von A. Wurtz, Strassburg, 1844, Vol. 1, pp. 142.

Kekulé. "Wir sind also zu der Ueberzeugung gelangt, dass die chemischen Verbindungen des Pflanzen-und Thierreichs dieselben Elemente enthalten wie die Koerper der leblosen Natur; wir haben die Ueberzeugung, dass in ihnen die Elemente denselben Gesetzen folgen; dass also weder in dem Stoff, noch in den Kraeften und ebensowenig in der Anzahl oder in der Art der Gruppirung der Atome ein Unterschied besteht zwischen den organischen und den unorganischen Verbindungen. Wir sehen eine fortlaufende Reihe chemischer Verbindungen, deren einzelne Glieder (wenn man nur die nahe liegenden vergleicht) eine so grosse Aehnlichkeit zeigen, dass naturgemaess nirgends eine Trennung gemacht werden kann. Wenn aber dennoch eine Trennung vorgenommen werden soll, wie sie in der That, einzig im Interesse der Uebersichtlichkeit, vorgenommen werden muss, dann ist diese Trennung an sich nicht natuerlich, sie ist rein willkuerlich und man kann eben darum die Grenze da ziehen, wo es gerade zweckmaessig scheint. Will man dabei so theilen, dass moeglichst das, was gewohnheitsmaessig in der organischen Chemie abgehandelt wurde, auch jetzt als besonderer Abschnitt abgehandelt werde, so erscheint es am zweckmaessigsten, wie dies in neurer Zeit schon oefter vorgeschlagen wurde, alle Kohlenstoffverbindungen in diesem Abschnitte zusammen zu fassen.

"Wir definiren also die organische Chemie als die Chemie der

Kohlenstoffverbindungen. Wir sehen dabei keinen Gegensatz zwischen unorganischen und organischen Verbindungen. Das was wir mit dem althergebrachten Namen organische Chemie bezeichnen und was man zweckmaessiger Chemie der Kohlenstoffverbindungen nennen wuerde, ist vielmehr nur ein specieller Theil der reinen Chemie, den wir desshalb besonders abhandeln, weil die grosse Anzahl und die besondere Wichtigkeit der Kohlenstoffverbindungen ein specielleres Kennenlernen derselben noethig erscheinen laesst."

Lehrbuch der organischen Chemie, vol. 1, p. 10. A translation of this page may be found in Roscoe and Schorlemmer, *Treatise on Chemistry*, vol. 3, Part 1, 32.

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THE ALKALOIDAL CONTENT OF STRAMONIUM LEAVES

BY

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The University of Wisconsin

CONTRIBUTIONS FROM THE COURSE IN PHARMACY

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INTRODUCTION

The daturas belong to the family *Solanaceae,* which yields such drugs as belladonna, stramonium, hyoscyamus, scopola, nicotiana (tobacco), and which is generally noteworthy for the alkaloids that have been isolated from its representatives. The daturas are no exception to the general rule. Of the thirty species and varieties of *Datura* recorded by Hooker and Jackson[1] seven are reported by Wehmer[2] as having been examined chemically, *viz:*

Datura Stramonium L.
Datura Metel L.
Datura quercifolia Hk. Bth. et Kth.
Datura meteloides D. C.
Datura Knightii (?)
Datura arborea L.
Datura fastuosa L. (*D. alba* Nees.)

Through the coöperation of Dr. R. H. True, at the time in charge of the Office of Drug Plant Investigations, Bureau of Plant Industry, Washington, D. C., and of Dr. William Trelease, at the time Director of the Missouri Botanical Gardens, seeds of a number of species and varieties were obtained for cultivation in the Northern Experiment Station at Madison, a coöperative experiment for the cultivation of medicinal plants by the U. S. Department of Agriculture and The University of Wisconsin. The results of these experiments, so far as cultivation of the plants and the harvesting of drugs are concerned, are recorded in the annual reports of the Government Expert in the immediate charge of the gardens. These reports are as yet unpublished but manuscript copies are on file with the Bureau of Plant Industry and The University of Wisconsin.[3]

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[1] *Index Kewensis,* Part I, p. 720; Supplements I, p. 128 and II, p. 56.

[2] *Die Pflanzenstoffe,* p. 690.

Whenever opportunity offered, alkaloidal assays were made of crude drugs. Thus a number of assays were made by M. E. Titus,[4] by H. O. Gray,[5] also by G. A. Russell,[6] the Government Expert.

Considerable material being on hand, it seemed highly desirable to utilize it for determining the alkaloidal content. The alkaloidal assays were undertaken from several points of view.

1.) It seemed desirable to ascertain the alkaloidal content of the leaf drug of a given species for a succession of years.

2.) A comparison of the alkaloidal content of the leaf drugs from different species and varieties was sought.

3.) A further comparison of the alkaloidal content of different parts of the leaf drug (stem, parenchymal tissue, etc.), as separated by the different degrees of fineness of a powder, likewise seemed desirable not only as a means of locating the alkaloid, but also as a possible means for the improvement of an inferior drug by pulverization and subsequent separation of the tissues by fractional sifting.

In the following account the alkaloidal assays bearing on the first proposition only are recorded.

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[3] See reports for 1908, 1909, 1910, 1911, 1912 and 1913.

[4] On the alkaloidal content of cultivated stramonium. U. W. thesis 1909.

[5] The alkaloidal content of cultivated and wild stramonium. U. W. thesis 1910.

[6] Personal communication from Washington, Bureau of Plant Industry.

THE ALKALOIDS AND ALKALOIDAL CONTENT OF THE SEVERAL SPECIES OF STRAMONIUM THAT HAVE BEEN EXAMINED CHEMICALLY

DATURA STRAMONIUM

This species yields both the leaf and seed drugs of a number of pharmacopoeias, hence has been examined repeatedly. A brief résumé of the literature on the chemical constituents has recently been compiled by Wehmer[2], who regards separately the chemistry of the several parts of the plant, *viz.*:

1.) Leaf.
2.) Root and stem.
3.) Seed (incl. germinated seeds)

This same order is here followed.

LEAVES

Hyoscyamine is the principal alkaloid, and is found in all parts of this organ. Presumably there are likewise present traces of atropine and scopolamine. In addition to these alkaloids, carotin *(Caroten)* has been found, also potassium nitrate. The inorganic constituents yield 17.4 p. c. of ash.

In the table which follows, the results of the numerous alkaloidal assays recorded in pharmaceutical and chemical literature have been compiled.

DATURA STRAMONIUM LEAVES.

Date	No.	Results	Assayer	Remarks
		p. c.		
1869	1	0.307	Guenther............	
	2	0.169	Guenther............	
1892	1	0.33	Thompson...........	
	2	0.42	Thompson...........	
	3	0.46	Thompson...........	
	4	0.35	Thompson...........	
	5	0.46	Thompson...........	
	6	0.32	Thompson...........	
	7	0.47	Thompson...........	
	8	0.45	Thompson...........	
	9	0.37	Thompson...........	
	10	0.46	Thompson...........	
	11	0.43	Thompson...........	
	12	....	....	Results of 31 samples previous to 1890 gave a maximum of 0.50 p. c., a minimum of 0.22 p. c. and an average of 0.36 p. c.
1894	1	0.139	Dohme...............	Keller's method used.
	2	0.085	Dohme...............	Dragendorff's methods used.
	3	0.654	Dohme...............	Collected in July. Gravimetric assay.
	3′	0.214	Dohme...............	Same sample. Volumetric assay.
	4	0.554	Dohme...............	Collected in July. Gravimetric assay.
	4′	0.231	Dohme...............	Same sample. Volumetric assay.
	5	1.420	Dohme...............	Collected in July. Gravimetric assay.
	5′	0.231	Dohme...............	Same sample. Volumetric assay.
	6	1.420	Dohme...............	Green leaves. Gravimetric assay.
	6′	0.271	Dohme...............	Same sample. Volumetric assay.
1894	1	0.3179	Beckurts............	Extraction according to Redwood, shaking out with chloroform.
	2	0.3179	Beckurts............	
	3	0.3083	Beckurts............	Extraction according to Redwood, shaking out with chloroform-ether. According to Schweissinger-Sarnow.
	4	0.3198	Beckurts............	
	5	0.362	Beckurts............	Digestion with acidified water, shaking out with chloroform.
	6	0.393	Beckurts............	
	7	0.3523	Beckurts............	Digestion with acidified water, shaking out with chloroform-ether.
	8	0.3082	Beckurts............	
	9	0.375	Beckurts............	Keller's method.

DATURA STRAMONIUM LEAVES—Continued.

Date	No.	Results	Assayer	Remarks
		p. c.		
1900	1	0.40	Schmidt	Average of many samples of cultivated leaves.
1903	1	0.20	Barclay	Home-dried sample.
1905	1	0.39	Schmidt-Feldhaus	
1905	1	0.310	......	Report Com. Adult. Penn. Ph. Ass'n.
......	2	0.350	......	
1906	1	0.458	Vanderkleed	Average of 9 lots. Only one assayed below 0.35 p. c.
1906	1	......	Puckner	"Range" of 16 samples: 0.13 to 0.45 p. c.
1906	1	0.24	......	Results of six different assayers of the same sample. Reported by Dohme.
	2	0.36	......	
	3	0.40	......	
	4	0.30	......	
	5	0.40	......	
	6	0.30	......	
1906	1	0.12	Farr-Wright	
	2	0.18	Farr-Wright	
	3	0.19	Farr-Wright	
	4	0.22	Farr-Wright	
	5	0.23	Farr-Wright	
	6	0.25	Farr-Wright	
	7	0.25	Farr-Wright	
	8	0.30	Farr-Wright	
1906	1	......	......	Average of small lots 0.458 p. c. Only one below 0.35 p. c. Report Com. Adult. Penn. Ph. Ass'n.
1907	1	......	Hankey	The average of the better lots was 0.25 p.c. Lowest 0.14 p.c.
1907	....	......	Kline-Graham	Seven lots out of 19 were below 0.35 p.c.
1907	1	0.318	Clark.	
	1'	0.320	Clark.	
	2	0.12	Clark	A microscopical examination, showed 2, 2', and 2" to be something other than stramonium.
	2'	0.000	Clark.	
	2"	0.07	Clark.	

DATURA STRAMONIUM LEAVES—Continued.

te	No.	Results p. c.	Assayer	Remarks
1908	1	0.15	Smith, Kline and French Co. Laboratories.	Eighteen samples were examined. Four were rejected as not being dried leaves of Datura stramonium. Only five shipments were accepted.
	2	0.15	Smith, Kline and French Co. Laboratories.	
	3	0.20	Smith, Kline and French Co. Laboratories.	
	4	0.18	Smith, Kline and French Co. Laboratories.	
	5	0.13	Smith, Kline and French Co. Laboratories.	
	6	0.17	Smith, Kline and French Co. Laboratories.	
	7	0.056	Smith, Kline and French Co. Laboratories.	
	8	0.24	Smith, Kline and French Co. Laboratories.	
	9	0.22	Smith, Kline and French Co. Laboratories.	
	10	0.25	Smith, Kline and French Co. Laboratories.	
	11	0.33	Smith, Kline and French Co. Laboratories.	
	12	0.29	Smith, Kline and French Co. Laboratories.	
	13	0.35	Smith, Kline and French Co, Laboratories.	
	14	0.27	Smith, Kline and French Co. Laboratories.	
1908	1	....	H. K. Mulford Laboratories.	Number of assays 25: average 0.34 p.c., lowest 0.13 p.c., highest 0.51 p.c.
1908	1	0.20	Evans Sons, Lescher and Webb.	Range of a year's samples.
	2	0.30	Evans Sons, Lescher and Webb.	
1909	1	0.37	Pearson.	
	2	0.23	Pearson.	

DATURA STRAMONIUM LEAVES—Continued.

Date	No.	Results	Assayer	Remarks	
	3	p. c. 0.22	Pearson.		
	4	0.34	Pearson.		
	5	0.28	Pearson.		
	6	0.30	Pearson.		
	7	0.25	Pearson.		
1909	1	0.24	Evans Sons.		
		0.208	Lescher & Webb.		
1909	1	....	Mulford's Laboratory................	Twenty four samples assayed: 19 assayed above 0.25 p. c., lowest 0.21 p. c., highest 0.33 p. c., average 0.34 p. c.	
	2	0.530			
1909	1	0.07	Dohme...............	Nine assayed, only one rejected.	
1910	1	....	Clark.................	All reports above 0.25 p. c., all below 0.35 p. c.	
1910	1	0.41	Patch		
	2	0.37	Patch		
	3	0.29	Patch		
	4	0.34	Patch		
	5	0.31	Patch		
	6	0.35	Patch		
1910	1	0.40	Engelhart...........	Only two out of 20 below 0.25 p. c.	
	2	0.45	....		
1910	1	0.19	Clark.................		
	1′	0.20	Clark.................		
	2	0.18	Clark.................		
	2′	0.17	Clark.................		
1911	1	0.361	Mitlacher & Wasicky	Collected July 5	From manured soil.
	2	0.321	Mitlacher & Wasicky	Collected July 21	
	3	0.332	Mitlacher & Wasicky	Collected August 2	
	4	0.298	Mitlacher & Wasicky	Collected August 27	
	5	0.397	Mitlacher & Wasicky	Collected Sept. 12	
	6	0.358	Mitlacher & Wasicky	Collected July 10	Natural soil.
	7	0.362	Mitlacher & Wasicky	Collected July 26	
	8	0.303	Mitlacher & Wasicky	Collected Aug. 18	Unmanured soil.
	9	0.236	Mitlacher & Wasicky	Collected Sept. 10	
	10	0.368	Mitlacher & Wasicky	Collected Sept. 14	

DATURA STRAMONIUM LEAVES—Continued.

Date.	No.	Results.	Assayer.	Remarks.
		p. c.		
1911	1	0.22	Clark, A. H..........	
	1'	0.21	Clark, A. H..........	
1912	1	0.14	Gane.................	Domestic stramonium.
	2	0.17	Gane.................	
1912	1	0.28	Patch................	
	2	0.198	Patch................	
	3	0.210	Patch................	
	4	0.41	Patch................	
1912	1	....	Scoville..............	9 below 0.26: 57 between 0.25 and 0.36: 36 between 0.36 and 0.45 p. c.: 8 above 0.45 p. c.
1912	1	0.47	Miller & Meader.....	
	2	0.55	Miller & Meader.....	
	3	0.52	Miller & Meader.....	
	4	0.46	Miller & Meader.....	
1913	1	0.50	Engelhardt...........	8 samples. All good quality.
1913	1	....	Kebler...............	Range of 32 lots of stramonium herb, 0.251 to 0 .451 p. c.
	2	0.21	Kebler............ ..	Stramonium herb.
	3	0.289	Kebler...............	Stramonium herb. contained 1 to 5 p. c. chestnut leaves.
	4	....	Kebler...............	Range of 43 lots of stramonium herb, 0.294 to 0.49 p. c.
	5	....	Kebler.....	Range of 1 lot of stramonium herb, 0.187 to 0.258 p. c.
1913	1	0.55	Miller and Meader..	Parent plant.
	2	0.50	Miller and Meader..	No's 2. 3, 4. 5. 6. individual plants, seed from No. 1. Without fertilizer.
	3	0.56	Miller and Meader..	
	4	0.50	Miller and Meader..	
	5	0.54	Miller and Meader..	
	6	0.42	Miller and Meader..	
	7	0.67	Miller and Meader..	No's 7, 8, 9, 10, 11, individual plants, seed from No. 1. Fertilizer used.
	8	0.66	Miller and Meader..	
	9	0.62	Miller and Meader..	
	10	0.65	Miller and Meader..	
	11	0.48	Miller and Meader..	
	12	0.46	Miller and Meader..	Parent plant.
	13	0.58	Miller and Meader..	No's 13, 14, 15, 16. individual plants, seed from No. 12. Without fertilizer.
	14	0.57	Miller and Meader..	
	15	0.63	Miller and Meader..	
	16	0.63	Miller and Meader..	
	17	0.64	Miller and Meader..	No's 17, 18, 19, 20, individual plants, seed from No. 12. Fertilizer used.

DATURA STRAMONIUM LEAVES—Continued.

Year	No.	Results.	Assayer.	Remarks.
	18	p. c. 0.68	Miller and Meader..	
	19	0.58	Miller and Meader..	
	20	0.71	....	
	21	....	....	Average of non-fertilized wild plants, 0. 28 p. c.
1914	1	0.491	Langenhan-Federer	1910 crop grown at Madison.
	2	0.460	Langenhan-Federer	1911 crop grown at Madison. Seed from 1910 crop.
	3	0.357	Langenhan-Federer	1912 crop grown at Madison. Seed from 1911 crop.
	4	0.299	Langenhan-Federer	1913 crop grown at Madison. Seed from 1912 crop.
	5	0.360	Langenhan-Federer	1913 crop grown at Madison. New seed.
	6	0.319	Langenhan-Federer	Individual plants, 1913 crop.
	7	0.425	Langenhan-Federer	Individual plants, 1913 crop.
	8	0.540	Langenhan-Federer	Individual plants, 1913 crop.
	9	0.203	Langenhan-Federer	Individual plants, 1913 crop.
	10	0.420	Langenhan-Federer	Individual plants, 1913 crop.
	11	0.360	Langenhan-Federer	Individual plants, 1913 crop.
	12	0.168	Langenhan-Federer	Picked in July, 1913.
	13	0.130	Langenhan-Federer	Picked in August, 1913.
	14	0.287	Langenhan-Federer	Picked in September, 1913.
	15	0.330	Langenhan-Federer	1911 crop grown in Milwaukee (H. G. Ruenzel).
	16	0.415	Langenhan-Federer	1912 crop grown in Milwaukee (H. G. Ruenzel).
	17	0.523	Langenhan-Federer	1913 crop grown in Milwaukee (H. G. Ruenzel).
	18	0.170	Langenhan-Federer	Commercial sample, whole leaf.
	19	0.241	Langenhan-Federer	Commercial sample, whole leaf.
	20	0.193	Langenhan-Federer	Commercial sample, whole leaf.

DATURA STRAMONIUM GIGANTEA

This variety is not included in the list of the species reported by Wehmer as having been examined chemically. The material used was raised in the medicinal herb garden of the Northern Station for the Cultivation of Medicinal Plants at Madison from seed obtained from the Missouri Botanical Garden. The material assayed was from four crops, *viz.*: those of 1910, 1911, 1912, and 1913.[7] In 1913 another crop from new seed was also harvested. The character of the alkaloids contained in these leaves has not been studied, but the leaves, when assayed according to the U. S. P., in 1913–'14, revealed the following alkaloidal content:

Crop of 1910	0.262	(Average of two assays)
1911 crop	0.175	“ “ “
1912 crop	0.265	“ four “
1913 crop	0.259	“ two “
1913 crop (new seed)	0.403	“ “ “

These results likewise do not admit of any satisfactory generalizations.

DATURA STRAMONIUM INERMIS

This variety also is not included in the list of species reported by Wehmer as having been examined chemically. The material used was likewise raised in the medicinal herb garden of the Northern Station for the Cultivation of Medicinal Plants at Madison from seeds obtained from the Missouri Botanical Garden. The material assayed was from four crops, *viz.*: those of 1910 to 1913 inclusive.[8] In 1913 leaves were also harvested from plants from new seeds. In collecting this last crop a distinction was made between plants having prickly pods and those having smooth pods. The character of the alkaloids contained in these leaves has also not yet been studied. When assayed in 1913–'14 according to the U. S. P. the leaves revealed the following alkaloidal content:

Crop of 1910	0.247	(Average of two assays)
Crop of 1911	0.496	“ “ “
Crop of 1912	0.446	“ “ “
Crop of 1913	0.240	“ “ “
Crop of 1913 (new seed, smooth pod)	0.333	“ “ “
Crop of 1913 (new seed, prickly pod)	0.417	“ “ “

The above results do not admit of any satisfactory generalizations.

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[7] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

[8] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

DATURA TATULA

The list of Datura species enumerated by Wehmer as having been examined chemically does not include this species which is known as the trumpet flower and which is reported as playing an important role in the poison literature of Mexico. Since Wehmer's book was published, an alkaloidal assay of the drug from this species has been reported upon by Miller and Meader,[9] who compare its alkaloidal content with that of *Datura Stramonium.*

The material used for the assays recorded below was raised in the medicinal herb garden of the Northern Station for the Cultivation of Medicinal Plants at Madison from seeds obtained from the Missouri Botanical Garden.

The material assayed was from three crops, *viz.*: those of 1911, 1912, and 1913.[10] The leaves were assayed in 1913–'14 according to the U. S. P.

Crop of 1911	0.334	(Average of two assays)
Crop of 1912	0.439	" " "
Crop of 1913	0.288	" " "
Crop of 1913 (new seed).............	0.453	" " "

DATURA TATULA INERMIS

This variety also does not appear to have been subjected to chemical examination heretofore. The material used was obtained from the medicinal herb gardens of the Northern Station for the Cultivation of Medicinal Plants located at Madison and was raised from seeds obtained from the Missouri Botanical Garden. The leaves, assayed in 1913–'14 for total alkaloids according to the U. S. P. 1900, were from the crops for 1911, 1912, and 1913[11] and gave the following results:

Crop of 1911	0.582	(Average of two assays)
Crop of 1912	0.552	" " "
Crop of 1913	0.259	" " "
Crop of 1913 (new seed).............	0.353	" " "

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[9] *Proc. of the Intern. Congress of Applied Chem.,* 17, p. 57.

[10] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

[11] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

DATURA INERMIS

Of this species there is also no record of previous chemical examination. The leaves examined for total alkaloids were obtained from the medicinal herb garden of the Northern Station for the Cultivation of Medicinal Plants located at Madison raised from seeds obtained from the Missouri Botanical Garden and were collected from the crops of 1910, 1911, 1912, and 1913.[12] When assayed in 1913–'14 for total alkaloids according to the U. S. P. 1900, they yielded the following results:

Crop of 1910	0.568	(Average of two assays)
Crop of 1911	0.560	" " "
Crop of 1912	0.676	" " "
Crop of 1913	0.390	" " "
Crop of 1913 (new seed)	0.145	" " "

DATURA METEL. L.

This species and the *D. Meteloides* have been subjected to chemical study by several investigators. Whether the work done in E. Schmidt's laboratory[13-16] was on *D. Metel.* L., or *D. Metel Moc. et. Sesse* does not become apparent from the original. *D. Metel Moc. et Sesse* is synonymous with *D. meteloides* D. C., q. v. Wehmer[14] supposes that Schmidt's work was done with *D. Metel* L. although he points out that de Plato,[15] who specifically mentions *D. Metel* L., found no alkaloid whatever but allantoin.

This species appears to have been examined first by E. Schmidt in 1903 who found principally l-scopolamine in the leaves (mean of assay 0.55 p. c)[13] The same alkaloid was found by Schmidt and Kirchner[16] in 1903 in the seeds, the calyx with the ovary, the corolla with the stamens, the stem, and the root. The seeds contained on the average 0.50 p. c. of alkaloid. In addition small amounts of hyoscyamine and atropine were found.[16]

Remarkable is the statement made more recently (1910) by de Plato that this species contains neither alkaloid nor glucoside.

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[12] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

[13] *Apt. Ztg.*, 18, p. 685; *Arch. d. Pharm.*, 243, p. 303.

[14] *Die Pflanzenstoffe*, p. 690.

[15] *Statz. Sperim. Agrar. Ital.*, 43, p. 79.

[16] *Arch. d. Pharm.*, 243, p. 309.

During the season of 1913 this species was included among the Datura experiments of the Northern Station at Madison[17]. Leaves of this crop assayed during 1913–'14 according to the U. S. P. yielded 0.445 of total alkaloids (average of two results).

DATURA LEICHARDTI

This is another species that has not been examined chemically, so far as the records show. The material in this case also was obtained from the medicinal herb garden of the Northern Station for the Cultivation of Medicinal Plants located at Madison, Wis. The leaves assayed during 1913–'14 according to the U. S. P. 1900 represented the crops of 1910, 1911, 1912, and 1913[18] and were picked from plants raised from seeds obtained from the Missouri Botanical Garden.

Crop of 1910	0.297	(Average of two assays)
Crop of 1911	0.286	" " "
Crop of 1912	0.490	" " "
Crop of 1913	0.312	" " "
Crop of 1913 (new seed)	0.380	" " "

DATURA QUERCIFOLIA

This species was subjected to an alkaloidal survey by Schmidt and Kircher[19] in 1905, who obtained their material from the Botanical Garden at Marburg. In the leaves and unripe fruits they found scopolamine and hyoscyamine together with little atropine. In the stem and roots they found scopolamine and hyoscyamine in about equal amounts and little atropine. In the leaves they found 0.41875 p. c. of total alkaloids. In the seeds hyoscyamine predominated. The seeds assayed 0.29279 p. c. of total alkaloids. The above results were obtained volumetrically, computed as scopolamine.

The material used for the assays recorded below were obtained from the Medicinal Herb Gardens of the Northern Station for the Cultivation of Medicinal Plants located at Madison, Wis. The plants have been raised from seeds obtained from the Missouri Botanical Garden. When subjected to the assay for total alkaloids during 1913–'14 according to the U. S. P. 1900, the leaves gave the following results:

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[17] See sixth annual report by the Government Expert of the Bureau of Plant Industry.

[18] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

[19] *Arch. d. Pharm.*, 243, 303.

Crop of 1910[20]	0.300	(Average of two assays)
Crop of 1911	0.420	" " "
Crop of 1913	0.286	" " "

D. FASTUOSA L. (D. ALBA NEES)

The alkaloidal content, according to Keller's method, was determined by Peinemann[21] in 1896, who found 0.41 p. c. Nagel[22] examined the drug in 1897. According to Hesse[23] (1898), the flowers contain principally scopolamine (0.51 p. c.), little hyoscyamine (0.03 p. c.) and atropine (0.01 p. c.). According to Brown,[24] 0.485 p. c. of scopolamine. Van der Driessen Mareeuw[25] (1898) records 0.149 p. c. hyoscyamine in the seeds. According to Shimoyama and Koshima[26] (1892), the seeds contain almost exclusively hyoscyamine (0.041 p. c.) and but little atropine (0.05 p. c.). According to the more recent investigations of Schmidt[27] (1906) the seeds contain principally scopolamine. The two horticultural varieties differ somewhat.

	"flor. coeruleis plenis"	"flor. albis plenis"
Scopolamine	0.216 p. c.	0.20 p. c.
Hyoscyamine	abt. 0.034 "	0.023 "
Atropine	traces	traces

The seeds are also reported as containing 11 p. c. of fatty oil. (v. d. Driessen Mareeuw[25].) Peckolt (1909) likewise reports on the chemical composition of the leaves and seeds. Leaves collected in 1913 at the Northern Station in Madison assayed 0.260 p. c. of total alkaloids (average of four assays).

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[20] See annual reports by the Government Expert of the Bureau of Plant Industry for the corresponding years.

[21] *Handelsbericht von Gehe & Co.*, 1896, p. 2.

[22] See Czapek, *Biochemie d. Pflanzen*, II, p. 316.

[23] *Annalen*, 303, p. 149.

[24] See Wehmer, *Die Pflanzenstoffe*, p. 691.

[25] *Nederl. Tijdschr. Pharm.* 11, p. 14.

[26] *Apt. Ztg.*, p. 458.

[27] *Arch. d. Pharm.*, 244, p. 68; *Apt. Ztg.*, 20, p. 669.

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1891.

Guenther, N., *Estimation of the alkaloids in the different parts of Atropa belladonna and Datura stramonium,* in *Pharm. Zeitsch. f. Russl.,* 8, p. 89. *Journn. de Chim. Med.*—p. 65; *Proc. A. Ph. A,* 19, p. 289; *Jahresber.,* 29, p. 53; Wittstein's *Vierteljahresschr.,* —, p. 598.

	Grams of fresh material used.	Percentage of moisture.	Percentage of daturine in dry substance.	Percentage of daturine in dry substances obt. by titration.
Root	34	63.7	0.065	....
Stem	50	70.8	0.063	....
Leaves	50	74.9	0.307	0.169
Seeds	50	29.8	0.365	0.318

Assay method. (See *Proc. A. Ph. A.*, 19, p. 289.)

1892.

Thompson, F. A., *Abstracts from Analytical Records* in *Proc. A. Ph. A.,* 40, p. 259.

The author reports on some of the results recorded in the records of the analytical laboratory of Parke, Davis & Co.

Eleven samples assayed by process No. 1 (Lyon's *Manual of Pharm. Assaying),* gave the following results: Stramonium leaves (p. 264). 0.33; 0.46; 0.42; 0.35; 0.46; 0.32; 0.47; 0.45; 0.37; 0.46; 0.43 per cent of crude total alkaloids; maximum, 0.47; minimum, 0.32; average 0.38. Thirty-one samples, examined during the five years previous to 1890, yielded a maximum of 0.5, a minimum of 0.22, and an average of 0.36 per cent.

Seed:—Fifteen samples assayed by process No. 1. yielded the following amounts of crude total alkaloids: 0.40; 0.36; 0.43; 0.45; 0.5; 0.36; 0.17; 0.22; 0.25; 0.31; 0.32; 0.24; 0.42; 0.38; 0.48 per cent. Maximum 0.5; minimum 0.17; average 0.35. The maximum of samples, examined previous to 1890, was: 0.65; minimum 0.3 and an average of 0.4 per cent.

1893.

Dohme, A. R. L., *The Relative Alkaloidal Value of the Various Parts of the Plant of Datura Stramonium* in *Am. Journ. Pharm.*, 65, p. 479.

After a discussion of the earlier work on stramonium assay by Guenther (1869), Trommsdorff, and E. Schmidt, and of the methods of Dragendorff, Lyons, and his own modification of Lyon's method, the author records the results of his own assays of leaves, stems, root, and seed.

1894.

Beckurts, H., *Wertbestimmung von Drogen und daraus hergestellten Praeparaten namentlich Extracten und Tincturen* in *Pharm. Centralh.*, 35, p. 566. *Apoth. Ztg.* 18, p. 110; *Pharm. Ztg.* 39, p. 676. *(Jahresber.*, 19, p. 26; *Proc. A. Ph. A.*, 43, p. 535.)

Folia Stramonii:—

(a) Extraction according to Redwood, shaking out with chloroform: 0.3179 p. c. and 0.3179 p. c. alkaloids.

(b) Extraction according to Redwood, shaking out with chloroform-ether according to Schweissinger-Sarnow: 0.3083 p. c. and 0.3198 p. c. alkaloids.

(c) Digestion with acidified water, shaking out with chloroform: 0.362 p. c. and 0.393 p. c. alkaloids.

(d) Digestion with acidified water, shaking out with chloroform-ether: 0.3323 p. c. and 0.3082 p. c. alkaloids.

(e) Process according to Keller: 0.375 p. c. alkaloids. (See also Beckurts, 1903).

1894.

Dohme, A. R. L., *Additional Experiments with Datura Stramonium,* in *Proc. A. Ph. A.*, 42, p. 231.

As a result of these additional experiments the author arrives at the following conclusions:

1.) "That the stems of Datura stramonium contain more alkaloid than the leaves."

2.) "That the plant Datura stramonium gathered in June contains less alkaloid than that gathered in July and August."

3.) "That Keller's method extracts more alkaloid from the drug Datura stramonium than Dragendorff's method does."

1896.

——— *Ostindische Drogen*, in *Handelsbericht von Gehe & Co.* 1896, p. 2.

Datura alba Nees (p. 6):—Dr. Peinemann obtained the following results according to Keller's method:—Seed, 0.541 p. c.; root, 0.315 p. c.; leaves, 0.41 p. c. alkaloids computed as atropine.

1899.

Van Driessen Mareeuw, W. P. H., *Untersuchung von Semen Daturae fastuosae Koetjoeboeng Kassan*, in *Nederl. Tijdschr. Pharm.*, 11, pp. 14, 51. *Chem. Centrb.*, 70 I, p. 539.

The author has examined the seeds of this plant, which he finds to contain 0.149 p. c. of hyoscyamine, and 10.9 p. c. of a fatty oil.

1900.

Schmidt, Ernst, *Ueber die quantitative Bestimmung des Alkaloidgehaltes der Blaetter von Datura Stramonium, Hyoscyamus niger und Atropa Belladonna*, in *Apoth. Ztg.*, 15, p. 13.

The author finds the average alkaloidal content of many samples of cultivated stramonium leaves to be 0.40 p. c. computed as atropine.

1903.

Barclay, J., *Notes on Crude Drugs, Fixed Oils, Waxes, etc. Eleventh Annual Laboratory Report of Messrs. Southall Brothers & Barclay, Limited.*, p. —, in *Pharm. Journ.*, 70, 207.

A home dried sample of stramonium leaves assayed 0.2 p. c. of alkaloid (titrated). A sample of seed assayed 0.3 p.

c. alkaloids. The authors are inclined to think that published figures place the average percentage of alkaloids in this drug somewhat high.

1903.

Beckurts, H., *Quantitative Bestimmung des Alkaloidgehaltes verschiedener starkwirkender Drogen und der aus diesen hergestellten Praeparaten VIII. Stramonium,* in *Apoth. Zeit.,* 18, p. 10. *Pharm. Journ.,* p. 425; *Proc. A. Ph. A.,* 51, p. 949.

So far as stramonium is concerned, the results recorded in this paper are the same as those recorded by the same author in 1894. (q. v.)

1905.

Schmidt, E., *Ueber die Alkaloide einiger mydriatisch wirkender Solanaceen,* in *Arch. d. Pharm.,* 243, p. 303.

1. Datura metel contains scopolamine as principal alkaloid.
2. Datura arborea contains scopolamine as principal alkaloid but also some hyoscamine.
3. Datura quercifolia contains scopolamine and hyoscyamine (leaves 0.4 p. c.; seeds 0.28 p. c.) in about equal amounts.
4. Datura stramonium contains mainly hyoscamine. See Schmidt & Kircher. 1905.
5. Atropa belladonna.

1905.

Schmidt, E. and J. Feldhaus, *Quantitative Untersuchung ueber die Verteilung des Alkaloides in den Organen von Datura Stramonium,* in *Arch. d. Pharm.,* 243, p. 328.

	p. c. alk.
The original seed "Ausgangssamen" contains....	0.33
The main root contains........................	0.10
The root branches contain.....................	0.25
The stem contains.............................	0.09

The branches "hoechster Ordnung" contain	0.36
The leaves contain	0.39
The "pistil" contains	0.54
The corolla contains	0.43
The calyx ("Kelchroehren") contains	0.30
The mature pericarps contain	0.082
The placenta of the ripe fruit contains	0.28
The mature seeds contain	0.48
The germs from the mature seeds contain	0.67
The assimilation tissue of the leaves contain	0.48
The middle and secondary nerves contain	1.39
The leaf stems contain	0.69

1905.

Schmidt, E. and A. Kircher, *Ueber die mydriatisch wirkenden Alkaloide einiger Daturaarten,* in *Arch. d. Pharm.,* 243, p. 309.

1. Datura metel:
    - a) Leaves cont. 0.55 p. c. of alk. computed as scopolamine.
    - b) Seeds cont. 0.50 p. c. of alk. computed as scopolamine.
2. Datura quercifolia:
    - a) Leaves cont. 0.418 p. c. of alkaloid.
    - b) Seeds cont. 0.292 p. c. of alkaloid.
3. Datura arborea:
4. Datura stramonium: A repetition of the work of Schmidt and Feldhaus, 1905 (q. v.)

1905.

——————., *Report of the Committee on Adulteration* in *Proc. A. Ph. A.*, 28, p. 47.

"Stramonium leaf: number of assays 2, lowest, 0.310 p. c., highest, 0.350 p. c., average, 0.33 p. c., general quality fair."

"Stramonium seed: number of assays 4, lowest 0.137 p. c., highest 0.257 p. c., average 0.214 p. c. General quality very good."

1906.

Dohme, A. R. L., *The Pharmacopoeia as a Legal Document*, in *Am. Dr. & Ph. Rec.*, 49, p. 267.

The author reports the amount of alkaloid found in the same sample of stramonium leaf, by the same process, by seven analysts to vary from 0.24 to 0.40 p. c.

1906.

Farr, E. H. and R. Wright, *Notes on Standardized Powdered Alcoholic Extracts*, in *Pharm. Journ.*, 76, p. 310.

1.) Alkaloids in Stramonium Seeds:—The authors review the results of Hurtz, E. Schmidt, Beckurts, Schweisinger, Lyons, Thompson, Parke, Davis & Co. and Umney. Their own results were:—0.16 p. c.; 0.17 p. c.; 0.16 p. c.; 0.19 p. c; 0.20 p. c.; 0.20 p. c.; 0.21 p. c.; 0.22 p. c.; 0.23 p. c.; 0.24 p. c.; 0.26 p. c; 0.28 p. c.; 0.28 p. c. alkaloids. Max. 0.28 p. c.; min. 0.16 p. c.; ave. 0.22 p. c.

2.) Alkaloid in Stramonium Leaves:—The authors review the results of Kordes, Umney, Parke, Davis & Co., and Thompson. Their own results were:—0.12 p. c.; 0.18 p. c.; 0.19 p. c.; 0.22 p. c.; 0.23 p. c.; 0.25 p. c.; 0.25 p. c.; 0.30 p. c. Max. 0.30 p. c.; min. 0.12 p. c.; ave. of eight samples 0.22 p. c. alkaloids.

After comparing the results of American chemists and European chemists they conclude that the stramonium leaves and seed grown in England contain less alkaloid than the American grown plant.

1906.

Vanderkleed, C. E., *Report of Committee on Adulterations*, in *Proc. Penn. Ph. A.*, 29, p. 120.

"Stramonium Leaf. Average assay of nine lots 0.458 p. c. of mydriatic alkaloids. Only one assayed below the required 0.35 p. c."

1906.

——————., *Report of Committee on U. S. Pharmacopoeia,* in *Proc. A. Ph. A.,* 54, p. 437.

Sixteen samples of stramonium (p. 440) assayed from 0.13 to 0.45 p. c. (Puckner).

1906.

——————., *Report of the Committee on Adulteration,* in *Proc. Penn. Ph. A.,* 29, p. 120.

"Stramonium leaf. Average assay of nine lots 0.458 p. c. of mydriatic alkaloids. Only one assayed below the required 0.35 p. c." (p. 124.)

1907.

——————., *Proc. Penn. Ph. A.,* 30, p. 55.

"Stramonium Leaf. Adulteration:—A sample of stramonium leaf on examination assayed only 0.056 p. c. of mydriatic alkaloids, whereas the U. S. P. standard calls for 0.25 p. c. The leaves, on close examination, differed from Datura Stramonium in many ways, both under the naked eye and with the microscope, and while we were unable to determine just what they were, we were satisfied they were not of the above mentioned official species. Reported by C. M. Kline and W. Graham." (p. 86.)

Stramonium Leaf

Standard 0.250

"Remarks—Seven lots out of nineteen were below the old standard of 0.35. Reduction of standard to 0.25 was probably a wise one." (p. 90.)

The report is respectfully submitted:—

Henry C. Blair,
P. Henry Utech,
E. Fullerton Cook,
Charles E. Vanderkleed."

1907.

Caspari, Chas. E., *Drug Adulterations*, in *Proc. Mo. Ph. A.*, **29**, p. 141.

"Stramonium seed:—Three samples examined, one O. K.; two weak. Stramonium leaf:—Three samples examined, three weak." (p. 147.)

1907.

Hankey, W. T., *The Assay Processes of the U. S. Pharmacopoeia VIII. (A report of the Chemist of Benton, Hall & Co.), in Am. Dr. & Ph. Rec.*, 50, p. 8.

The author has assayed lots of stramonium which fell as low as 0.14 p. c.; the average of the better lots running close to 0.25 p. c. of mydriatic alkaloids.

1908.

——————., *Report of Committee on Adulteration*, in ***Proc. Penn. Ph. A.***, 31, p. 65.

"The following illustrations are taken from actual results obtained in the laboratory of Smith, Kline & French Company, since August, 1906, and are submitted for your consideration, to illustrate the irregularities of the drug market."

"Stramonium:—Eighteen samples were examined. Four samples were not the dried leaves of Datura Stramonium and were promptly rejected. Nine samples were below the U. S. P. standard of 0.25 per cent, the total mydriatic alkaloids found being 0.15 p. c., 0.15 p. c., 0.20 p. c., 0.18 p. c., 0.13 p. c., 0.17 p. c., 0.056 p. c., 0.24 p. c., and 0.22 p. c. The shipments accepted contained 0.25 p. c., 0.33 p. c., 0.29 p. c., 0.35 p. c. and 0.27 p. c. of mydriatic alkaloids." (p. 79.)

1908.

Bernegau, L. H., *Some Remarks on the Adulterations of Drugs and Chemicals as Found in Practice*, in ***Am. Journ. Pharm.***, 80, p. 221.

The author reports on a sample of stramonium leaf, containing an average of 0.262 p. c. of alkaloids. On closer examination the sample was found to consist of a mixture of stramonium and hyoscyamus.

1908.

Evans Sons, Lescher & Webb, *Stramonium Leaves,* in *Analytical Notes,* 3, p. 39.

"Between 0.2 p. c. and 0.3 p. c. of alkaloid were found in the year's samples."

1908.

————., *Report of the Committee on Adulteration,* in *Proc. Penn. Ph. A.,* 31, p. 65.

"The following results were obtained from the summary of drug assays made in the analytical laboratory of the H. K. Mulford Company during the year ending June 1st, 1908: "Stramonium leaf: No. of assays twenty-five, lowest 0.130 p. c., highest 0.510 p. c., average 0.341 p. c., standard 0.25 p. c. mydriatic alkaloids." (p. 88.)

1909.

————., *Report of the Committee on Adulterations,* in *Proc. Penn. Ph. A.,* 32, p. 119.

Of twenty-four samples of "stramonium leaf" examined by H. K. Mulford Company during the year ending June 1, 1909, the lowest assayed 0.210 p. c., the highest 0.530 p. c., average 0.347 p. c. 19 assayed above the standard of 0.25 p. c., 5 below.

Of seven samples of "stramonium seed" the lowest assayed 0.201 p. c., the highest 0.434 p. c., average 0.297 p. c. 5 assayed above, 2 below the standard of 0.25 p. c.

1909.

Dohme, A. R. L. and H. Engelhart, *Purity of Some Official and Non-official Drugs and Chemicals,* in *Proc. A. Ph. A.,* 57, p. 713.

Stramonium leaves (p. 718). "The samples submitted were of a very good quality, as out of nine only one had to be rejected, which assayed only 0.07 p. c. of total mydriatic alkaloids."

1909.

Evans Sons, Lescher & Webb, *Analytical Notes,* 1909, p. 54.

Two consignments of stramonium are reported as yielding 0.24 and 0.208 p. c. of alkaloids.

1909.

Pearson, W. A., *The Quality of Pharmaceuticals from June 1, 1908, to June 1, 1909,* in *Proc. Penn. Ph. A.,* 32, p. 177.

Stramonium: "The seven lots assayed contained 0.37 p. c., 0.23 p. c., 0.22 p. c., 0.34 p. c., 0.28 p. c., 0.3 p. c., and 0.25 p. c."

1910.

——————., *Report of Committee on Adulterations,* in *Proc. Penn. Ph. A.,* 33, p. 131.

Of twenty-four samples of stramonium leaves examined by H. K. Mulford Company during the year ending June 1, 1910, the lowest assayed 0.274 p. c., the highest 0.501 p. c., average 0.386 p. c., all above the standard of 0.25 p. c.

1910.

——————., *Report of the Committee on Drug Market,* in *Proc. A. Ph. A.,* 58, p. 739.

Stramonium:—"Not one sample was up to the original 0.35 p. c. All met 0.25 p. c." (A. H. Clark, p. 747.)

"Has been found considerably adulterated with chopped chestnut leaves, and large shipments have been rejected for this reason. If stramonium leaves are pure and good they will assay 0.35 per cent, and 0.3 per cent should be insisted on." H. H. Rusby. (p. 747.)

"Six samples assayed 0.41; 0.37; 0.29; 0.34; 0.31; 0.35; per cent. E. L. Patch." (p. 747.)

1910.

Chevalier, J., *Influence de la culture sur la teneur en alcaloides de quelques Solanées*, in *Comptes Rendus*, 150, p. 344.

With the aid of proper fertilizer, the author increased the alkaloidal content of spineless Datura stramonium from an average of 0.100 to 0.125 p. c. (ordinary cultivation and fertilization) (?) to 0.200 p. c. (fertilized with nitrates?)

1910.

Engelhardt, H., *Quality of some Crude Drugs Examined During 1909*, in *Proc. A. Ph. A.*, 58, p. 1256.

Only two out of twenty samples of stramonium (p. 1258) examined by the author assayed below the official standard, while fully 70 p. c. assayed much higher, e. g. 0.40 to 0.45 p. c. total alkaloids.

1910.

Sayre, L. E., *Do Pharmacists Properly Regard the Official Standards?* in *Proc. A. Ph. A.*, 58, p. 1093.

The author in his discussion presents a report of drugs and medicines analysed by the drug laboratories of the Kansas State Board of Health, Kansas University, in which six out of seven samples of stramonium (p. 1098) examined were illegal, only one sample answering to the requirements.

1911.

——————., *Report of Committee on Drug Market*, in *Proc. Penn. Ph. A.*, 34, p. 117.

Stramonium leaf:—p. 132.

No. of assays, 1. Result, 0.330 of mydr. alk's. From H. K. Mulford's laboratory report for year 1911.

1912.

——————., *Report of the Committee on Drug Market*, in *Proc. Penn. Ph. A.*, 35, p. 165.

Stramonium leaves:—p. 180.

No. of assays 11, lowest 0.189 p. c., highest 0.470 p. c., ave. 0.305 p. c. of mydr. alk's.

From H. K. Mulford's laboratory report for year ending June 1, 1912.

1912.

——————., *Report of Committee on Drug Market,* in *Journ. A. Ph. A.,* 1, p. 499.

"Stramonium:—Two lots of domestic stramonium assayed 0.17 p. c. and 0.14 p. c. alkaloids (E. G. Gane, p. 503); 0.198 p. c., 0.21 p. c., 0.41 p. c., 0.28 p. c., E. L. Patch." (p. 503).

1912.

Dohme, A. R. L. and H. Engelhardt, *Drug Quality During the Period 1906-1911,* in *Journ. A. Ph. A.,* 1, p. 99.

"Stramonium Seed:—Very little variation was noticed in the alkaloidal percentage of this drug."

"Stramonium Leaves:—There was no reason for reducing the standard from 0.35 p. c. to 0.25 p. c. since shipments with more than 0.35 are easily available. Only very few samples with less than 0.3 p. c. were met with. The quality of the drug was almost alike during the six years."

1912.

Miller, F. A. and Meader, J. W., *The Alkaloidal Content of Individual Plants of Datura Stramonium and Datura Tatula L,* in *The 8th Intr. Cong. Applied Chem.,* 17, p. 57.

The author reviews the work of Meyer, Hesse, Peineman, Kircher, Feldhaus, Farr and Wright, Kordes, Umney, Smith, Kline and French, Vanderkleed, Hankey, Puckner, and Lilly laboratories. Their own results obtained from cultivated plants were:

Datura stramonium, 0.47 p. c., 0.55 p. c., 0.52 p. c., 0.46 p. c. alkaloids.

Datura Tatula 0.63 p. c., 0.65 p. c., 047 p. c. alkaloids.

1912.

Scoville, W L., *On Drug Standards*, in *Journ. A. Ph. A.*, 1, p. 1338.

"Stramonium Leaf:—

9 below	0.26 p. c.
57 between	0.25 and 0.36 p. c.
36 between	0.36 and 0.45 p. c.
8 above	0.45 p. c.
110 assays.	

1913.

——————., *Report of Committee on Drug Market*, in *Proc. Penn. Ph. A.*, 36, p. 77.

Stramonium leaf:—p. 96.

No. of assays 14, lowest 0.170 p. c., highest 0.618 p. c., ave. 0.297 p. c of mydr. alk's.

From H. K. Mulford's laboratory report for year ending June 1, 1913.

1913.

Engelhardt, H., *Purity of Chemicals and Drugs*, in *Journ A. Ph. A.*, 2, p. 163.

"Stramonium: Eight samples were examined and were found to be of good quality. Some assaying nearly 0.5 p. c. of mydriatic alkaloids. There was no good reason for reducing the standard of this drug."

1913.

Miller, F. A., *Breeding of Medicinal Plants*, in *Am. Journ. Ph.*, 85, p. 291. *(The Lilly Scientific Bulletin*, 4, p. 127.)

The author reports the alkaloidal content of the "parent plant" and its "offspring."

"Selections of *Datura tatula* varied from 0.47 to 0.65 p. c. alkaloids. Of 10 individuals from the plant yielding 0.47 p. c. alkaloids, a range of from 0.44 p. c. to 0.57 p c. was obtained, the average for the ten being 0.51 p. c. Of the same number of individuals from the plant yielding 0.65 p. c. a range of 0.43 p. c. to 0.77 p. c. was obtained, the average being in this case 0.65 p. c."

"A mixed sample of leaves from uncultivated plants of *Datura tatula* gave a yield of only 0.35 p. c."

"The average yield of commercial stramonium as noted for the past three years is 0.34 p. c."

Datura Stramonium cultivated the past year gave yields of 0.46 and 0.55 p. c. alkaloids.

Datura humulis flava. Mixed sample 0.42 p. c. alkaloids.

Datura ferox. Individual selections from 0.53 p. c. to 0.70 p. c. alkaloids.

1913.

Miller, F. A. and Meader, J. W., *The Assay of Individual Plants of Datura stramonium, Datura tatula, and Other Species and Varieties,* in *Journ. Ind. E. Chem.*, 5, p. 1014. *(Lilly Scientific Bulletin,* 4, p. 156.)

A report on the alkaloidal content of individual plants, raised from seeds of individual plants, and of the effect of fertilizers on *Datura stramonium, D. tatula* and *D. ferox.* Also a comparison of the alkaloidal content between wild and cultivated plants of *D. stramonium and D. tatula.*

1913.

—————., *Report of the Committee on Drug Market,* in *Journ. A. Ph. A.,* 2, p. 1081.

"Stramonium Herb. Six lots gave ash 14.7 p. c. to 19 p. c. Thirty two lots gave alkaloid 0.251 p. c. to 0.451 p. c. One lot was low, 0.21 p. c. One contained from 1 p. c. to 5 p. c. chestnut leaves. Assay ash 25.15 p. c., alkaloid 0.289 p. c." (p. 1106.) L. F. Kebler.

"Stramonium Leaves. One lot contained 10 p. c. of adulterant. Probably leaves of a species of prunes. Forty-three lots gave alkaloid from 0.294 p. c. to 0.49 p. c. The alkaloidal standard (0.25 p. c.) may be a little low. One lot gave ash 20.5 p. c. moisture 6.9 p. c., alkaloid 0.294 p. c. One lot gave 0.187 p. c. to 0.258 p. c. alkaloid" (p. 1106.)

L. F. Kebler.

1914.

Miller, M. S., *Influence of Soil Composition on Medicinal Plants,* in *Journ. A. Ph. A.,* 3, p. 308.

By way of summary and comparison the author quotes average results from one of his earliest papers (1913.)

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BULLETIN OF THE UNIVERSITY OF WISCONSIN
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A CHEMICAL STUDY OF THE OILS OF SEVERAL SPECIES OF EUPATORIUM

AND

A STUDY OF THE CHEMICAL AND PHYSICAL PROPERTIES OF WISCONSIN WORMWOOD OIL

BY

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CONTRIBUTIONS FROM THE COURSE IN PHARMACY

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A CHEMICAL STUDY OF THE OILS OF SEVERAL SPECIES OF EUPATORIUM

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A STUDY OF THE CHEMICAL AND PHYSICAL PROPERTIES OF WISCONSIN WORMWOOD OIL

BY

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CONTRIBUTIONS FROM THE COURSE IN PHARMACY

MADISON, WISCONSIN
1914

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A CHEMICAL STUDY OF THE OILS OF SEVERAL SPECIES OF EUPATORIUM

The composites to which the genus *Eupatorium* belongs are represented by approximately 12,000 species of which more than 500 belong to the genus under consideration. Of these 500 species probably ten have been examined chemically more or less.

The chemistry of the composites includes a considerable number of representatives of the following phytochemical groups: alkaloids, glucosides, bitter principles, carbohydrates, volatile oils. Yet none of these, save possibly levulin and inulin, can be regarded, even in a measure, as characteristic of the family.

In the more restricted field of the genus *Eupatorium,* which comprises more species than do some of the botanical families, the situation at present is not very different. As already pointed out, only a fraction of one per cent of the known species has been submitted to any chemical examination whatever. Of these, only three *(Eupatorium capilifolium, E. triplinerve,* and *E. aromaticum)* have yielded volatile oils thus far. The principal interest in the volatile oils at present centers in the dimethyl ether of hydrothymoquinone which is reported to constitute about 75 to 80 p. c. of the ayapana oil *(E. triplinerve).* Before having been found in ayapana oil, this ether was known to exist only in the oil from arnica root, another composite plant.

Of the 500 or more species of *Eupatorium,* most of which are native to warm and tropical climates, 56 are indigenous to the United States. Although in the warmer regions the genus is represented by a few annuals and shrubs, it is composed in the main of perennial herbs. Some of these grow abundantly, hence invited investigation. Inasmuch as up to the present time no method has been devised of separating certain phytochemical constituents as conveniently as the volatile constituents are separated by steam distillation, the preliminary chemical survey of the genus was restricted to the study of the volatile oils. For this purpose five species were distilled with the result that two volatile oils were obtained.

As already pointed out one of the principal objects of interest in the chemical study of the genus lay in the discovery of hydrothymoquinone dimethyl ether by Semmler in *E. triplinerve.* This same substance has since been found in *E. capillifolium.* The interest in the chemical study of this genus is enhanced by the medicinal use to which about a dozen of the species are put, principally in this country, but in other countries as well. Several species have been granted official pharmacopoeial recognition (*E. perfoliatum* and *E. purpureum*), but these apparently owe their medicinal value to other constituents than the dimethyl ether referred to, or any other volatile constituents that might find their way into volatile oils.

The following account comprises the results of a chemical investigation of several southern as well as northern species of *Eupatorium* that has extended over about ten years and includes the following species:

Eupatorium capillifolium
E. purpureum
E. hyssopifolium
E. perfoliatum
E. serotinum

EUPATORIUM CAPILLIFOLIUM (LAM.) SMALL. (E. FOENICULACEUM WILD.)

INTRODUCTION

This species grows from Delaware to Florida and Louisiana, from the mountain region to the coast, in low fields, pastures and open woods; but is most abundant in the damp coast plain. It grows also in Cuba and other islands of the West Indies. Under the most favorable conditions for growth it attains a height of about ten feet, but generally is from three to six feet high. It is paniculately much branched, the leaves are very numerous, mostly alternate, blades much compound, the segments linear-filiform to filiform, corolla white.

It is commonly known as Dog Fennel and Hog Weed. In some localities it is known as Mare's Tail, and in others as Texas Cedar.

According to the *Tallahassee Floridian* (1861) Isaac Bierfield of Newberry, S. C., obtained good results with this plant as a tanning material, but F. P. Porcher[1] states that he examined the plant and found scarcely a trace of tannin in it.[2]

Culbreth *(Materia Medica)* states that its juice relieves pain from insect bites.

In 1896 Schimmel & Co. reported as follows upon a sample of the oil distilled by Mr. E. Moulié of Jacksonville, Fla.:

"Light yellow color and sharply aromatic, somewhat pepper-like odor, not at all resembling that of the true fennel or anethol. Sp. gr. at 15°C is 0.935, optical rotation in 100 mm. tube is $+17°50'$. Contains an abundance of phellandrene."

In their report of Nov. 1908 the same firm reports as follows:

"Pale yellow oil from flowering herb, yield about 0.1 p. c.; $d_{15°}$ 0.926; $a^{D}+18°30'$; ester number 7.11. Gives cloudy solution with 3.5 or more volumes of 90 p. c. alcohol. High phellandrene content."

DISTILLATION OF THE OIL

Almost every year since 1903 I have distilled an oil from plants of this species growing in the vicinity of Auburn, Ala. The material first distilled was identified by Professor F. S. Earle.

In all about 30 samples of oil were obtained, the time of collecting the material extending in the main from about the middle of September to the middle of October. Since the oil reported by Schimmel & Co. was dextrorotatory and all my samples were levorotatory, it was decided to distill the plant at various periods to see if a dextrorotatory oil could be obtained.

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[1] *Resources of the Southern Fields and Forests*, p. 414.

[2] An aqueous infusion of the dried plant gives a decided coloration (bluish black) with a solution of ferric chloride.

The first distillation was made May 1st when the plants were about ten inches high. The stems were broken off near the ground and the entire plant distilled. Later when the plants were large a considerable part of the lower portion of the stem was rejected. In such cases the yield of oil would vary considerably by rejecting or including the stems which are heavy and contain but little oil. In the case of large plants the stem was broken off on the average about fifteen inches above the ground. The material was usually distilled in the green state.

In the following table are given the time of collection, the yield of oil, the sp. gr., index of refraction, rotation in a 100 mm. tube, percentage of methoxy group, saponification number, saponification number after acetylating, the acid number and the percentage of thymohydroquinone dimethyl ether calculated from the percentage of methoxyl.

From the table it will be seen that the yield in case of sample No. 1 was 0.36 per cent and that the yield gradually increased to the maximum of 1.11 p. c. in case of sample No. 9, distilled Nov. 16. In several other cases a yield of about 1.35 per cent was obtained but these samples were not studied. The yield of 0.61 p. c. for sample No. 11 was from material collected after one or two light frosts.

Beginning with the sp. gr. 0.9392 in case of oil No. 1 there is a decrease until the minimum 0.9195 is reached in oil No. 4; from this point on there is a gradual increase to 0.96004 in the case of oil No. 11.

The index of refraction for sample No. 1 is 1.504479; there is then a gradual decrease to 1.497808 for sample No. 4. From this there is a gradual increase to 1.506887 for sample No. 10. Then a slight decrease for sample No. 11.

All oils distilled before September have dextrorotation; all distilled in September and after have levorotation. Omitting No. 2 there is a gradual increase in dextrorotation from +10.27° in case of sample No. 1 to +14.29° in the case of sample No. 4. There is then a decrease to +10.02° for sample No. 5 and it is reasonable to suppose that at some time between July 30 and September 8 an optically inactive oil might have been obtained. From No. 6 on there is a rather gradual increase in levorotation.

However, it should be stated here that oils distilled only one day apart have shown as great differences in rotation as that between No. 6 and No. 8.

A glance at the table will show that the percentage of methoxyl is rather high, namely 18.42 for sample No. 1, and then gradually decreases to 14.79 for sample No. 4 and that there is then a gradual increase to 21.45 in the case of sample No. 10, that for No. 11 being slightly lower.

The saponification numbers of the oils, also the saponification numbers after acetylation show an increase reaching the maximum in sample No. 5. Although these values were not determined for all the samples, the data obtained show a diminution in these values for the oils distilled later.

The few acid numbers determined show nothing that would throw light upon the relative composition of the oils.

Table I

When distilled	Yield Per cent.	Sp. gr. $\frac{25^\circ}{25^\circ}$	$n_{D_{27^\circ}}$	a_D for 100 mm tube.	p. c. OCH_3	Saponification No.	Sapon. No. after acetylating	Acid No.	p. c. of thymohydroquinone dimethyl ether
1 May 1, 1912....	0.36	0.93919	1.504479	+10.27	18.42	5.6	12.94	0 207	57.63
2 May 13, 1912....	0.47	0.9326	1.502330	+ 7.47	16.87	6.4	13.26	0.206	52.78
3 May 25, 1912....	0.51	0.92378	1.500732	+13.82	15.92	5.38	10.61	....	49.81
4 June 27, 1912....	0.527	0.91950	1.497808	+14.29	14.79	9.45	43.72	....	46.02
5 July 30, 1912....	0.567	0.9269	1.49875	+10.02	16.20	16.68	56.85	....	50.91
6 Sept. 3, 1911....	0.960	0.9278	1.499886	− 6.33	....	13.67	....	0.18	52.13
7 Sept. 13, 1911....	0.99	0.9346	1.501014	− 8.20	16.66	12.26	23.85	....	....
8 Oct. 27, 1911....	1.02	0.9472	1.505866	−13.99	20.16	....	....	0.25	63.08
9 Nov, 16, 1911....	1.11	0.9505	1.506143	−11.77	20.61	10.53	....	0.10	64.49
10 Nov. 23, 1911....	1.03	0.9577	1.506887	−11.73	21.45	14.43	30.95	....	67.11
11 Dec. 3, 1912....	0.613	0.96004	1.506422	−16.70	21.24	10.60	23.83	....	66.46

PROPERTIES OF THE OIL

The oil prepared from fresh material is generally almost colorless, or of a very light yellow color. That from material which has been dried and kept for some time is usually more highly colored. The odor is somewhat pepper-like but not very sharply aromatic. The yield from fresh material collected in September and early October varied from 0.8 p. c. to 1.35 p. c., being generally above 1 p. c. The optical rotation for oils distilled at the above-named period varied from —3.7° to —16.8° in a 100 mm. tube, though in one case it was as high as —30.1°. The sp. gr. determined at 25°C with water at 25°C as standard varied from 0.9278 to 0.9472; the index of refraction determined at 20°C varied from 1.50055 to 1.50688. Acid numbers obtained for oils distilled in September and October were 0.18 and 0.25 respectively. For oil distilled in September the saponification numbers 10.92, 11.2, and 13.67, respectively, were obtained.

Concentrated nitric acid (70 p. c.) acts energetically upon the oil with production of a reddish brown color. Concentrated sulphuric acid also reacts readily with the oil, producing a similar result. In both cases the degree of color depends upon the relative amounts of oil and acid mixed. Concentrated solutions of alkali carbonates have no apparent effect upon the oil. Cold concentrated aqueous solution of caustic alkali has no apparent effect but on heating produces a yellowish color. With an alcoholic solution of caustic potash the oil is slowly colored, and by heating on the water bath it becomes very dark brown.

Like volatile oils generally, it dissolves readily in ether, chloroform, benzene, acetic ether, and petroleum ether.

With a small amount of alcohol the oil forms a clear mixture, but when more alcohol is added a point is soon reached where the mixture becomes turbid,[8] remaining so even after the addition of a large volume of alcohol. It shows the same behavior towards methyl alcohol and glacial acetic acid.

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[8] Other oils are known which show a similar behavior. For instance Kobuschi oil dissolves in 1.2 to 10 volumes of 80 p. c. alcohol but when highly diluted with 80 p. c. alcohol the solution becomes turbid. Gildemeister und Hoffmann, *Die aetherischen Oele*, vol. II, p. 388.

Oil of Champaca flowers is soluble in one volume of 80 p. c. alcohol but when more than 7 volumes of the 80 p. c. alcohol have been added the solution becomes opalescent. The same oil is soluble in 2 volumes of 70 p. c. alcohol but the addition of 4 volumes or more produces decided turbidity. *Ibidem*, II, p. 392.

One volume of the oil dissolves in about 0.7 volumes of 90 p. c. alcohol, but when a little more of the alcohol is added it becomes turbid and remains so even after the addition of 50 volumes of the 90 p. c. alcohol.

EXAMINATION FOR ALDEHYDES AND KETONES

With Schiff's reagent the oil gave no reaction, indicating the absence of aldehydes.

Tested with phenyl hydrazine according to directions given by Mulliken[4] (in test VII—2) there was a very slight opacity. 5 cc. of oil heated with 40 p. c. solution of neutral sodium sulphite in an aldehyde flask gave a slight diminution in volume. From the results it may be stated that ketones are either absent or present in only very slight amount.

EXAMINATION OF THE OIL FOR PHENOLS

In order to determine if phenols were present in appreciable amount 5 cc. of oil were placed in an aldehyde flask, 5 p. c. KOH solution added in small amounts, shaking after each addition, and the flask then filled with water. There was no apparent diminution in the volume of the oil.

The oil was then treated in the usual way for removing phenols, using a 4–5 p. c. solution of potassium hydroxide. There was obtained about 0.11 p. c. of a very thick reddish-brown liquid with a slightly acrid, bitterish taste. With alcoholic ferric chloride there was scarcely any change of color noticeable, but on addition of water a slight purplish color was observed, an indication of the presence of salicylic acid.

IDENTIFICATION OF METHOXYL

In order to determine if a methoxy compound was present some of the original oil was heated with concentrated hydriodic acid according to Perkin's[5] modification of Zeisel's method, with the exception that the tube leading the liberated methyl iodide to the silver nitrate solution extended below the surface of the liquid. A generating flask with a neck about 16 inches long was used. For one experiment about 12cc. of hydriodic acid and 3cc. of acetic anhydride were used. The flask was heated in a glycerin bath at 140°–145° C. A blank test gave no precipitate in the silver nitrate solution, showing that both the condenser and vessel containing red phosphorus could safely be omitted. In the quantitative determinations the silver iodide, after evaporation of the alcohol, was transferred to a Gooch crucible, washed and dried to constant weight at 130°C. The percentage of methoxyl found was 16.66 p. c.

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[4] *Identification of Pure Organic Compounds*, vol. I, test VII–2.

[5] *Jour. Chem. Soc.* 1903, p. 1367.

In order to remove all doubt as to whether the group present in the oil was the OCH_3 group or the OC_2H_5 group the alkyl halide was passed into an alcoholic solution of dimethyl aniline. After a short time a white crystalline substance separated from the alcoholic solution. After purification by re-crystallization from alcohol this compound had the melting point of 213°–214°. The melting point of trimethyl phenyl ammonium iodide, the compound which would have been formed in the above experiment if the oil had contained a methoxy group, is 211°–212°[6] If, on the other hand the oil contained the ethoxy group there would have been formed dimethyl ethyl phenyl ammonium iodide which melts at 124.5°–126°[7].

Analyzed for iodine by Stepanow's method[8] 0.3085 gm. of the substance gave 0.2765 gm. of silver iodide. This corresponds to 48.42 p. c. of iodine. The theoretical amount of iodine for trimethyl phenyl ammonium iodide is 48.23 p. c.

In another experiment the alkyl halide obtained by using the fraction of oil boiling at 244°C. was passed through a condensing tube surrounded by ice. A small amount of a heavy, slightly reddish colored liquid with an odor suggesting methyl iodide collected in the receiver. When distilled it passed over almost completely at 42°–43°C.

These experiments may be considered proof of the presence of the OCH_3 group and the absence of the OC_2H_5 group.

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[6] Feist, *Ber.* 33, p. 2094, (1900)

[7] Claus and Howitz, *Ber.* 17, p. 1325 (1884)

[8] *Ber.* 39, p. 4056 (1906)

FIRST FRACTIONATION OF THE OIL

In 1904 a sample of the oil was freed from phenol, dried and fractionated, without previous saponification, under a pressure of 8–10 mm.

Under the attending circumstances it was not possible to pursue the work far, but notwithstanding its incompleteness the results are recorded here in order to compare them with those of the corresponding fractions of other samples of the oil.

The rotation was determined in a 100 mm. tube at 20°C. in a Laurent polariscope, using sodium light.

Table II

Fraction.	Boiling point.	Rotation.
1	Below 58°	+43.2°
2	58–65°	+43.5°
3	65–75°	....
4	75–95°	+12.8°
5	95–100°	– 0.7°
6	100–110°	– 3.7°
7	110–115°	–10.5°
8	115–120°	–15.9°
9	120–125°	–21.5°
10	125–130°	–28.5°
11	130–135°	–32.0°
12	135–143°	–29.0°
13	143–160°	– 7.1°
14 Residue		

Fraction No. 1. had a sp. gr. of 0.83134 at $\frac{20^\circ}{20^\circ}$

An elementary analysis gave the following results:

0.1754 gm. of the substance gave 0.1844 gm. H_2O = 11.68 p. c. H. and 0.5628 gm. CO_2 = 87.5 p. c. C.

Computed for $C_{10}H_{16}$: H = 11.76 and C = 88.23.

The first four fractions together constitute about 15 p. c. by volume of the original oil.

Fraction No. 1. when distilled under ordinary pressure came over at 165° to 170° C.

Fraction No. 8. Sp. gr. = 0.97334 20°/20°. Analysis: 0.1878 gm. gave 0.5201 gm. CO_2 = 75.73 p. c. C and 0.1650 gm. H_2O = 9.78 p. c. H.

Fraction No. 9. Sp. gr. = 0.97543 at 20°/20°. Analysis: 0.2253 gm. gave 0.6194 gm. CO_2 = 74.98 p. c. C and 0.1944 gm. H_2O = 9.59 p. c. H.

Fraction No. 10. Sp. gr. 0.97406 20°/20°. Analysis; 0.2040 gm. gave 0.5718 gm. CO_2 = 76.44 p. c. C and 0.1806 gm. H_2O = 9.83 p. c. H.

Fraction No. 11. Sp. gr. 0.96879 20°/20°. Analysis: 0.2185 gm. gave 0.6184 gm. CO_2 = 77.18 p. c. C and 0.1986 gm. H_2O = 10.09 p. c. H.

Fraction No. 12. Analysis: 0.1430 gm. gave 0.4055 gm. CO_2 = 77.33 p. c. C and 0.1332 gm. H_2O = 10.32 p. c. H.

Fraction No. 13. Analysis: 0.1342 gm. gave 0.3902 gm. CO_2 = 79.30 p. c. C and 0.1372 gm. H_2O = 11.35 p. c. H.

RESIDUE: This residue was very thick and hardened on cooling. To remove it from the flask the following were tried successively; alcohol, absolute alcohol, methyl alcohol, ether, acetone, strong alkali solution, nitric acid, glacial acetic acid,—all without apparent effect. After washing with alcohol it was heated on a water bath with absolute alcohol. This loosened it from the flask but apparently dissolved little or none of it. It was then treated with chloroform in which it dissolved readily. This solution was added to alcohol with stirring. The substance was thrown out of solution, then washed with alcohol and dried. It formed a white, light, odorless, tasteless powder, similar in appearance to light calcined magnesia.

Analysis: 0.1230 gm. gave 0.3796 gm. CO_2 = 84.17 p. c. C and 0.1232 gm. H_2O = 11.12 p. c. H.

Computed for $(C_{10}H_{16})x$, C = 88.23; H = 11.76.

Computed for $C_{20}H_{32}O$, C = 83.33; H = 11.11.

FRACTIONATION OF THE OIL WITH STEAM

The oil from which the phenols had been removed was then saponified by boiling for one hour on a water bath with about an equal volume of half normal alcoholic potassium hydroxide solution. After washing until alkali was no longer present, 500 cc. of oil were distilled with steam, using as a fractionating column a plain glass tube three feet long, and about ¾ inch internal diameter. Owing to the bumping occasioned by the viscid character of the oil, it was not possible to apply much heat to the flask, consequently it was necessary to discontinue distillation quite often in order to siphon off the water which had condensed in the flask.

In this way there was some loss of oil. The oil drawn off was quite milky even after standing 24 hours. Fractions of 200 cc. each were made and the oil removed from each by means of a separatory funnel. The rate of distillation was about 90 drops per minute. Usually five or six fractions were obtained before discontinuing distillation. The following fractions were obtained, together with a small amount of a thick reddish-brown residue.

The following table shows the amount of oil obtained from each 200 cc. of distillate, with the sp gr., optical rotation and index of refraction for each fraction of oil. As will be noticed from the table the first fraction of oil obtained on renewing the distillation was considerably larger than the one just preceding it.

Table III

No. of fraction.	No. cc. of oil	Density $\frac{25°}{25°}$	$\alpha_{D25°}$	$n_{D25°}$
1	59.5	0.84916	+50.35	1.477400
2	41.0	0.86629	+42.65	1.482962
3	28.0	0.88979	+29.28	1.488762
4	20.5	0.91691	+ 9.07	1.496110
5	15.7	0.93670	− 6.25	1.501390
6	15.1	0.94455	−12.40	1.503062
7	15.9	0.94794	−14.84	1.503328
8	14.9	0.95179	−17.62	1.504665
9	13.5	0.95474	−20.14	1.505222
10	12.3	0.95731	−22.75	1.505774
11	11.1	0.95945	−24.98	1.506422
12	12.0	0.96050	−25.44	1.506701
13	11.1	0.96220	−27.28	1.507256
14	10.9	0.96376	−29.22	1.507440
15	10.5	0.96461	−30.55	1.507716

No. of fraction.	No. cc. of oil	Density $\frac{25°}{25°}$	α_D	$n_{D25°}$
16	10.0	0.96671	−31.56	1.507900
17	11.2	0.96681	−31.90	1.508084
18	10.0	0.96765	−33.40	1.508268
19	9.8	0.96763	−34.96	1.508452
20	9.5	0.96837	−35.80	1.508636
21	9.2	0.96856	−36.61	1.508636
22	9.4	0.96854	−37.28	1.508728
23	9.0	0.96837	−38.75	1.508820
24	9.5	0.96831	−39.55	1.508820
25	8.7	0.96809	−40.75	1.508820
26	8.5	0.96791	−41.70	1.508820
27	8.5	0.96789	−42.18	1.509096
28	8.0	0.96749	−43.07	1.509096
29	7.8	0.96645	−45.05	1.509096
30	8.0	0.96599	−46.06	1.509096
31	7.8	0.96491	−47.90	1.509096
32	7.0	0.96340	−49.80	1.509004
33	7.0	0.96256	−50.85	1.509004
34	5.7	0.96184	....	1.508452
35	5.0	0.96164	....	1.508268
36	3.5	0.96164	....	1.508084
37	2.0	0.96323	....	1.507256
38	1.5	....	....	....
39	1.0	....	....	....
40	0.8	0.968603	....	1.507348
41	0.4			
42	0.3			
43	0.2			

SEPARATION OF TERPENES BY DISTILLATION WITH ALCOHOL

Since Fendler[9] succeeded in separating reasonably pure pinene from oil of Cascarilla bark by distillation with alcohol, it was decided to apply the same method to this oil. Accordingly a mixture of 500 c. c. of oil and 500 c. c. of 95 p. c. alcohol was distilled on a water bath until about 500 c. c. of distillate were obtained, then 500 c. c. more of alcohol were added to the flask and the distillation continued until another 500 c. c. of distillate were obtained. The alcoholic distillates were separately mixed with a large volume of water, the oil which separated removed and washed with water. This addition of alcohol and distillation was continued in the same manner until the amount of oil removed by one distillation was very small. In obtaining the twelfth fraction absolute alcohol was used; the total volume of distillate was 490 c. c. and the amount of oil separated was 12 c. c., considerably less than that obtained with 95 p. c. alcohol.

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[9] *Arch. der Pharmacie* 238, p. 682.

In the following table is given the amount of oil separated by each distillation, together with the optical rotation and the index of refraction for each fraction of oil.

Table IV

No. of fraction.	Amt. c. c. of distillate.	Amt. c. c. of oil.	Rotation in 100 mm. tube.	Index of refraction.
1	505	27.00	+55.5°	1.477988
2	515	21.5	+55.8	1.478184
3	520	15.5	+53.6	1.479845
4	510	13.5	+52.1	1.480820
5	512	10.5	+42.3	1.484220
6	505	9.5	+40.2	1.485578
7	515	7.7	+35.3	1.488186
8	505	6.5	+26.4	1.493640
9	500	5.5	+15.01	1.494115
10	518	4.5		
11	515	3.5	−5.03	1.500074
12	490	1.2		
13	510	3.5		
14	520	3.0		
15	510	2.7		

Another 500 c. c. of the same sample of oil were mixed with 500 c. c. of absolute alcohol and distilled as before. In this case three fractions of oil were obtained, the first two by use of absolute alcohol, the third by using 95 p. c. alcohol.

Table V

Fraction.	Vol. of fraction.	Rotation in 100 m.m. tube.
1	14.0 cc	+52.25°
2	13.5 "	+53.40°
3	18.0 "	+52.30°

From the above tables it will be seen that terpene of a comparatively high degree of purity may be separated from this oil by a single distillation with alcohol. It also seems to be true that a purer terpene can be obtained by using 95 p. c. alcohol. The rotations of the first three fractions obtained by distillation with 95 p. c. alcohol were +55.5°,+55.8°, and +55.63° respectively. When another portion of the same oil was fractionated with steam the first three fractions showed a rotation of +50.35°, +42.65° and +29.28° respectively. From these results it seems that a purer terpene can be separated by alcohol vapor than by steam.

By reference to tables given below it will be seen that repeated fractionation of the oil under diminished pressure gives fractions in which the rotation rises, reaching its maximum in the one case in the second, and in the other case in the third fraction. The same result, though in a lesser degree, is noticed in both distillations with alcohol, while in the case of steam distillation the rotation rapidly diminishes.

FRACTIONATION OF THE OIL

The residue from the 500 c. c. of oil which had been subjected to distillation with alcohol was washed with water, dried with fused sodium sulphate, and together with the fractions obtained by the distillation with alcohol, was fractionated three times under diminished pressure (23 mm.). Then all the fractions boiling above 85° under 23 mm. pressure were fractionated twice at ordinary pressure.

Fourteen fractions and several residues were obtained. The oil used in this fractionation was not saponified. In the following table is given the amount of each fraction, also the optical rotation in 100 mm. tube, the index of refraction at 19°C., and the sp. gr. at 25°C. for each fraction. In the last column is given the percentage of methoxyl in each fraction except the first two which gave practically no reaction for methoxyl. The methoxyl determinations were made by a modification of the Zeisel method described on another page.

Table VI

	Boiling point.	Pressure.	Amt. of fraction. cc.	Rotation at 20° C.	Index of refraction.	Sp. gr. $\frac{25°}{25°}$	P. C of methoxyl.
1	70-72°	23 mm	55	+58.0°	1.4741	0.831	.....
2	72-75°	"	21	+66.2°	1.4757	0.834	.....
3	75-85°	"	32	+64.6°	1.4782	0.838	0.99
4	180-190	760	5.5	+49.9°	1.4842	0.872	3.78
5	190-200° }	"	7.0	+34.4°	1.4916	0.947	9.26
6	200-210° }						
7	210-220°	"	14.5	+ 3.25°	1.5024	0.935	16.09
8	220-225°	"	14.0	— 0.05°	1.5045	0.947	17.96
9	225-230°	"	24.5	— 0.43	1.5050	0.954	20.36
10	230-235°	"	27.5	— 0.20°	1.5054	0.963	21.67
11	235-240°	"	34.0	+ 0.10°	1.5071	0.972	24.00
12	240-245°	"	85.5	+ 1.20°	1.5086	0.977	24.26
13	245-250°	"	15.5	+ 3.50°	1.5077	0.971	22.60
14	250-260°	"	9.0	+ 5.20°	1.5057	0.971	18.53

SAPONIFICATION AND FRACTIONATION OF THE OIL

Since some of the fractions obtained in the first fractionation of the oil were rather small for identification and also for comparison with the results obtained by fractionation with and without previous saponification of oil, 1500 c.c. of oil were boiled an hour and twenty minutes on a water bath with an equal volume of semi-normal alcoholic potassium hydroxide. The mixture was then poured into a large volume of water, the oil separated and washed, dried with anhydrous sodium sulphate, and then fractionated five times under a pressure ranging from 16 mm. to 25 mm. The following fractions were obtained.

Table VII

Fraction.	Boiling point.	Amt. of fraction.	α_{D27°	$d\frac{25^\circ}{25^\circ}$
1	-65°	50 c. c.	+44.10°	0.834
2	65-66°	60 "	+56.98°	0.832
3	66-67°	62 "	+68.92°	0.829
4	67-70°	28 "	+66.70°	0.833
5	70-80°	18 "	+46.18°	0.844
6	80-100°	10 "	+17.85°	
7	100-105°	43 "	—1.07°	
8	105-110°	....	—1.54°	
9	115-116°	46 "	—1.25°	
10	115-120°	66 "	—1.74°	
11	120-125°	62 "	—4.55°	
12	125-130°	85 "	—5.80°	
13	120-135°	84 "	—8.15°	
14	135-138°	120 "	—11.20°	
15	138-139°	107 "	—14.01°	
16	139-141°	116 "	—20.43°	
17	141-142°	75 "	—28.55°	
18	135°	38 "	—45.54°	
19	135-155°	34 "	—53.50°	
Small residue	....	....	....	

With exception of the first six, the above fractions were then distilled once under ordinary pressure. In the following table are given the boiling point, quantity, optical rotation in 100 mm. tube, density at $\frac{25^\circ}{25^\circ}$ and the index of refraction at 29° for each fraction. The percentage of methoxyl is given for four fractions. The amount which distilled below 210° was very small.

Table VIII

Boiling point	Quantity	Rotation in 100 mm. tube	Sp. gr. $\frac{25^\circ}{25^\circ}$	Index of refraction	p. c. of OCH_3
210–213°........	60 c. c.	–1.70°	0.931	1.4970	15.36
213–216°........	60 "	–1.35°	0.932	1.4981	
216–221°........	60 "	–1.10°	0.934	1.4986	
221–231°........	35 "	–0.53°	0.951	1.5028	
231–238°........	15 "	–0.50°	....	1.5038	
238–243°........	60 "	–0.06°	0.976	1.5049	
243–244°........	120 "	+0.30°	0.984	1.5065	25.34
244°........	120 "	+0.74°	0.983	1.5067	26.40
244–245°........	120 "	+1.17°	0.981	1.5065	
245–246°........	108 "	+1.65°	0.978	1.5058	
246–248°........	44 "	+2.50°	0.972	1.5054	22.41
248–252°........	30 "	+3.65°	0.968	1.5048	
252–258°........	....	+4.84°	0.961	1.5042	
Residue.......	....	....	....	....	

LOW BOILING HYDROCARBONS

The physical properties of the first fractions obtained from all the samples of oil fractionated indicate that this portion of the oil consists almost entirely of hydrocarbons. This was proved beyond question by an elementary analysis of fraction No. 1 given in Table II. But in those cases where the oil was repeatedly fractionated the low-boiling fractions have a somewhat lower specific gravity than that of any of the known terpenes. The lowest specific gravity reported for a terpene is probably that for sabinene, namely 0.8400 at 20°C., and that for d-α-phellandrene, 0.8440 at 19°C. The first fraction of oil mentioned in Table II was found to have the specific gravity 0.8313 at 20°C; a very low specific gravity was also found for fraction No. 3, given in Table VII, 0.8295 at 25°C.

In view of these low specific gravities it is possible that some hydrocarbon besides terpene is present in these fractions.

A small amount of one of the unsaturated aliphatic hydrocarbons, myrcene or ocimene, mixed with the phellandrenes could give specific gravities such as those reported in Table VII for the low boiling fractions. Contradictory to this explanation, however, is the fact that the lowest specific gravities recorded in Table VII, namely 0.8295 coincides with the highest rotation, +68.92°. The rotation would be lowered by the presence of myrcene, since it is optically inactive.

With reference to the index of refraction it will be seen that the values recorded for the first three fractions in Table VI, for the first two in Table IV and for the first one in Table III all agree reasonably well with those for the phellandrenes, the lowest recorded in the literature being 1.4732 at 19°C for d-α-phellandrene from elemi oil, the highest being 1.4788 at 20°C for d-β-phellandrene from water fennel oil.

On the other hand the optical rotation for some of the low-boiling fractions recorded in Tables VI and VII is higher than that for any dextro-phellandrene so far reported, the highest being +60°21′ given by Gildemeister and Stephan[10] for a preparation from Schinus oil. The highest rotation reported in this paper is +80.2° for fraction No. 5, Table IX.

IDENTIFICATION OF PHELLANDRENES

Using the method of Wallach,[11] nitrosites were prepared from fractions No. 1, 2, 3, and 4, Table VII. The compounds were purified by dissolving them in chloroform and precipitating by means of methyl alcohol. A beautiful soft white mass of silky needles was obtained from each fraction. The yield was small and gradually diminished from fraction No. 1 to No. 4.

The amount of nitrosite obtained from 30 c. c. of each fraction and the melting point of each were as follows:

	Gm.	m. p.
Fraction No. 1	2.52	111–112°
Fraction No. 2	2.22	113–114°
Fraction No. 3	1.98	112–113°
Fraction No. 4 (from 15 c. c.)	0.92	112–114°

No attempt was made to prepare a nitrosite from fractions No. 5 and 6, but No. 7, when treated in the usual way, gave no nitrosite. The nitrosites were dissolved in chloroform and the optical rotation taken in a 100 mm. tube at 23°C.

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[10] *Arch. der Pharmacie,* 235, p. 591.

[11] *Annalen,* 246, p. 282.

Percentage strength of solutions was 10.

Specific gravity of solutions 1.46 at 23°C.

The following values were obtained.

$\alpha_{D23°}$—40.7° for fraction No. 1.
" —65.7° for fraction No. 2
" —76.7° for fraction No. 3.
" —99.3° for fraction No. 4.

In order to obtain further material for the identification of phellandrenes by the preparation of the nitrosites the low boiling portion of another sample of oil was repeatedly fractionated under a pressure of about 26 mm. The following table gives the boiling point and optical rotation of each fraction, together with the melting point of the nitrosite prepared from each fraction:

Table IX

Fraction	Boiling point	Rotation	m. p. of nitrosite.
1	69-70°	+41.0°	100-101°
2	70-72°	+47.1°	96- 97°
3	72-73°	+68.7°	97- 98°
4	73-75°	+72.9°	97- 98°
5	75-77°	+80.2°	100-101°
6	77-80°	+75.0°	100-101°

In determining these melting points the temperature was raised very slowly. By somewhat more rapid heating they all melted at 112–113°. In optical rotation these nitrosites showed very different results from the first ones prepared. Whereas those first prepared were all levorotatory those from the second sample of oil showed dextrorotation for the first three fractions, and slight levorotation for the fourth. In the last case several readings were taken at intervals of several hours. The rotation gradually diminished from –0.4° to –0.12°. Owing to lack of time the rotation of the nitrosites from the other fractions could not be determined.

Considering the physical properties of the low-boiling portion of this oil and the formation of the nitrosite there can scarcely be any doubt that at least one of the phellandrenes is present.

EXAMINATION FOR PINENE

In the case of every sample of oil which was repeatedly fractionated and even in those cases where the oil was fractionated but once by means of alcohol vapor, fraction No. 1 had a lower dextrorotation than the fractions immediately following. The rotation of fraction No. 1 in the various samples of oil fractionated varied from +44.1° to +58°. A small portion of fraction No. 1, table VI was distilled under ordinary pressure. The temperature rose rapidly to about 160°C and a considerable portion of the fraction distilled between 160° and 165°C. The rotation of the distillate was +54° in a 100 mm. tube. The rotation was thus very much reduced by one distillation but owing to evidence of decomposition the fraction was not redistilled. The fact that a part of this fraction distilled between 160° and 165° is positive proof that some hydrocarbon other than a phellandrene is present in the oil. The boiling point of the phellandrenes so far as reported is variously given as 173° to 176°C.

A small amount of dextro-α-pinene mixed with dextro-α-phellandrene would have the effect of lowering the boiling point, the rotation, and the index of refraction and raising the specific gravity.

An attempt was made to prepare a nitrosochloride from the lowest boiling fraction by the method of Wallach but with a negative result.

Inasmuch as the highly optically active pinenes yield little or no nitrosochloride, some of fraction No. 1 of this oil was mixed with an equal volume of a low boiling fraction from oil of *Pycnanthemum Tullia* having a rotation of —44° and this mixture was treated in the usual way for the preparation of the nitrosochloride. The result here was also negative.

So far as boiling point is concerned β-pinene might be present in fraction No. 1, but it can be excluded on the ground of its higher specific gravity, namely 0.8675.

EXAMINATION FOR SABINENE

For this hydrocarbon the following constants have been reported: b. p. 162°–166°; sp. gr. at 20°C 0.840 to 0.842; rotation in a 100 mm. tube +63 to +67.5°; index of refraction 1.4660 to 1.4678. These constants agree fairly well with those of fraction No. 1 of the oil under investigation here, except that the rotation given for sabinene is considerably higher, that is almost 20° higher than the lowest rotation obtained for fraction No. 1, table VII. However, results obtained by Schimmel & Co.,[12] in the fractionation of a larger amount of sabinene from oil of savin may be considered a very strong indication of the presence of sabinene in fraction No. 1 of this oil. 20 p. c. of the sabinene in question boiled between 162° and 163°, had the sp. gr. 0.8481 at 15°C, and the rotation in a 100 mm. tube +59°30′.

EXAMINATIÓN FOR LINALOOL

Fractions boiling above 190°C were repeatedly fractionated, first under diminished pressure and then under ordinary pressure.

A few c. c. of oil were obtained between 195° and 206°C. In order to determine if linalool were present this fraction was oxidized with chromic acid mixture; almost immediately an odor suggesting that of oil of lemon was developed. After shaking the mixture thirty minutes it was made slightly alkaline and then subjected to steam distillation. A pleasant smelling, light yellow oil was obtained. Judging from the odor that citral was probably present as the result of oxidation, an attempt was made to prepare the semicarbazone by the method of Tiemann.[13] 5 c. c. of the fraction dissolved in 30 c. c. of glacial acetic acid were mixed with 4 gms. of semicarbazide hydrochloride dissolved in a little water. Almost immediately a white solid separated. This was filtered out and found to be soluble in water. Washed with methyl alcohol and dried it was found to have the m. p. 169–170° with decomposition. Semicarbazide hydrochloride and glacial acetic acid alone gave a white precipitate which melted with decomposition at 170°C. The white compound obtained from the oxidation product of the fraction boiling at 195–200°C was, therefore, not a semicarbazone but unchanged semicarbazide hydrochloride.

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[12] Gildemeister u. Hoffman, *Die aetherischen Oele,* vol. II, p. 301.

[13] *Ber.* 31, p. 3331; and 32, p. 115.

Another portion of the oxidized fraction was treated with cyanacetic acid by the method of Tiemann[14] for the preparation of citralidenecyanacetic acid but no condensation product could be separated.

With Schiff's reagent the oxidation product behaved almost exactly like citral. In neither case was a pink color produced, in fact no coloration was produced at once, but a purple color was slowly formed.

A further test was applied by heating 5 c. c. of the oxidized fraction with 40 p. c. solution of neutral sodium sulphite on a water bath. The reaction of the mixture and a slight diminution in volume of the oil indicated the presence of a small amount of aldehyde or ketone. Although the evidence is rather slight it is, nevertheless, considered quite probable that the oil contains a small amount of linalool. All fractions boiling between 195° and 220° yield by oxidation oils which have an odor suggestive of citral. The color of the products from the lower boiling fractions is light yellow, the color gradually becomes darker with the higher boiling products and finally is deep red, due to the presence of thymoquinone which results from the oxidation of thymohydroquinone dimethyl ether.

IDENTIFICATION OF BORNEOL

The fraction boiling at 206°–208° was oxidized with chromic acid mixture in the same manner as was the fraction boiling at 195°–200°C. This product was then treated by the method of Emil Fischer for the preparation of camphoroxime. The product after re-crystallization from dilute alcohol was almost colorless. It melted at 116° to 117°C. The m. p. of camphoroxime is given as 117°–119°. The m. p. and odor of the product obtained are in agreement with those of camphoroxime. To determine if the oxime obtained might have resulted from camphor present as such and which might have escaped oxidation, some of the original fraction was treated with hydroxylamine hydrochloride in the same manner as the oxidized fraction. No oxime could be separated, though the odor of the mixture suggested that traces of camphor might be present.

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[14] *Ber.* 31 p. 3329.

The fraction boiling at 208°–212° was oxidized in the same manner as was the fraction boiling at 206°–208° and an oxime prepared from the product. The oxime obtained had about the same melting point as that obtained from the preceeding fraction, but the yield was larger as might be expected, since the boiling point of borneol is 210°–212°C.

From the oxidation product of this fraction a semicarbazone was prepared as follows: 2 gm. of semicarbazide hydrochloride, 2 gm. of potassium acetate and 6 c. c. of water were mixed with 12 c. c. of the oxidized liquid and allowed to stand about three weeks. A small amount of a slightly yellowish substance separated which melted at about 201°C. Camphor semicarbazone melts at 236°–238°, thymoquinone semicarbazone at about 193° C. The substance obtained was evidently a mixture of the two semicarbazones mentioned.[8]

To learn more about the composition of this fraction it was acetylated and the acetylated oil saponified. The acetylation was carried out in the usual manner, the mixture being boiled gently during one hour. In saponification the liquid was boiled on a water bath one hour. A saponification number of 64.6 was obtained. Estimated as an alcohol of the composition $C_{10}H_{18}O$, this would correspond to about 18.67 p. c. alcohol. The small yield of camphor oxime obtained as stated above goes to show that some other alcohol besides borneol is present.

This portion of the oil was fractionated so often it was thought there could not be more than traces of the dimethyl ether of thymohydroquinone present. However, a methoxy determination was made to throw light upon this point. 0.7100 gm. of the fraction gave by the usual method 0.7428 gm. AgI, corresponding to 13.8 p. c. OCH_3 which is equivalent to 43.19 p. c. of thymohydroquinone dimethyl ether. This would leave a considerable part of the fraction unexplained as to composition.

In order to determine if hydrocarbons might still be present an elementary analysis of the fraction was made.

0.3324 gm. of the substance gave 0.2773 gm. H_2O and 0.9444 gm. of CO_2 corresponding to 9.26 p. c. H and 77.48 p. c. C. This result makes it very improbable that a hydrocarbon in appreciable amounts could be present. And thus the composition of a considerable portion of the fraction still remains unexplained. If an alcohol which is decomposed by long boiling with acetic anhydride, such as linalool, be present this would possibly account for the remaining portion of the oil.

This fraction shows a very characteristic reaction with concentrated nitric acid. When treated with a small amount of concentrated nitric acid it is decomposed with the formation of a blue or bluish-green liquid, the color of which, if the right amount of nitric acid is used, persists for a long time when exposed to the air. This reaction was tried with linalool, terpineol and borneol each by itself and also in solution in thymohydroquinone dimethyl ether, but no color similar to that of the fraction of oil could be obtained. It is, therefore, quite evident that there is in this fraction some compound still unaccounted for and that at least one alcohol besides borneol is present.

Fraction 220°–225°. Some of this fraction was acetylated and then saponified, whereby a saponification number of 18.26 was obtained which corresponds to 5.09 p. c. of alcohol of the composition $C_{10}H_{18}O$.

An elementary analysis gave the following result: 0.2696 gm. of substance gave 0.2362 gm. H_2O and 0.7724 gm. of CO_2. Found $C=78.13$, $H=9.73$. Computed for an alcohol of the formula $C_{10}H_{18}O$: $C=77.92$, $H=11.68$.

Computed for the dimethyl ether of thymohydroquinone, $C_{12}H_{18}O_2$: $C=74.22$, $H=9.27$. Since borneol was identified in the fraction boiling at 208°–212° and since the main constituent of the oil quantitatively, is the dimethyl ether of thymohydroquinone which boils at about 245°C it is quite certain that both of these compounds are present in this fraction, the latter predominating. But the high percentage of carbon makes it certain that some compound with a higher carbon content is present.

IDENTIFICATION OF THYMOHYDROQUINONE DIMETHYL ETHER

The physical and chemical properties of the high boiling portions of the oil, especially the fraction boiling at 244°C. suggested the presence of methyl eugenol. Accordingly a portion of this fraction was oxidized with potassium permanganate as follows: About 30 c. c. of the fraction were heated in a large flask with about 1200 c. c. water to 50°C. on a water bath, and to this 24 gm. of $KMnO_4$ were added in small portions, with thorough shaking. When the liquid was decolorized it was filtered, the filtrate reserved, the precipitate, which still contained unchanged oil, was returned to the flask, mixed with 600 c. c. water, and 12 gm. more of $KMnO_4$ were then added in the same manner as before. This mixture was filtered, the filtrate united with the first one and evaporated on a water bath to a small volume. The liquid was then acidified and shaken out with ether. After distilling off the ether there remained a small amount of a thick, syrupy mass, with a slight odor of valerianic acid. After long standing no crystals were formed. The next higher boiling fraction was subjected to the same treatment, but with the same result.

The above described treatment was successfully applied by Petersen[15] to a high boiling portion of the oil of *Asarum europaeum* for the identification of methyl eugenol by conversion of the latter into veratric acid. It was also successfully applied by me to a high boiling fraction of the oil of *Asarum arifolium*[16] for the identification of methyl eugenol.

In a further attempt to identify methyl eugenol in this oil, a bromination test which had yielded the tribromderivative of methyl eugenol when applied to a high boiling fraction of the oil of *Asarum arifolium*[17] was also applied here as follows:

About 8 gm. of the fraction boiling at 244°C. were dissolved in chloroform. To this solution, kept cold in a freezing mixture, a chloroformic solution of bromine was added drop by drop, with constant shaking, until a slight excess of bromine had been added. After evaporation of the chloroform by a current of dry air, a thick brown colored mass remained from which no crystals could be obtained even after long standing. The same test was applied to the next higher boiling fraction, but with the same negative result. From these results it was concluded that methyl eugenol is not a constituent of the oil.

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[15] *Arch. d. Pharm.* 1888, 113.

[16] *Ibid.* 240, 380.

[17] *Ibid.* 240, 382.

After all attempts to establish the presence of methyl eugenol had failed, the only other known methyl ether, namely the dimethyl ether of thymohydroquinone, which agrees reasonably well in physical and chemical properties with the fraction boiling at 244°C., was taken into consideration.

The residues obtained by heating the fraction with concentrated hydriodic acid in order to establish the nature of the alkoxy group present, were not examined until after the absence of methyl eugenol had been reasonably well proved. When these were examined the nature of the ether present was at once shown. After standing a short time a solid body had formed in these acid residues. This was filtered out and washed with water in which it was found to be almost insoluble. The substance was thus obtained almost white. As it was found to be quite soluble in boiling water it was recrystallized from that solvent. It melted at 142°C. According to Carstanjen[18] thymohydroquinone melts at 139.5°C., and according to Ciamician and Silber[19] it melts at 143°C.

When oxidized with chromic acid mixture it yielded a reddish yellow substance of irritating odor, almost insoluble in water, readily soluble in alcohol and having the melting point 44°–45°C. In all these characteristics it agrees perfectly with thymoquinone which results upon oxidation of thymohydroquinone.

It is thus seen that the test which proved the alk-oxy group to be methoxyl, at the same time proved that the high boiling methyl ether present is the dimethyl ether of thymohydroquinone.

Further proof of the correctness of this conclusion was obtained by oxidation of the high boiling fractions. The portion of the oil boiling in the neighborhood of 200°C was oxidized with chromic acid mixture, in the first place, in order to ascertain the nature of the alcohol present. The liquid thus obtained was of a light yellow color characteristic of oil of lemon. All the fractions boiling above 200°C. were next oxidized in the same way, and it was found that there was a gradual change in the color of the products obtained, passing from the light yellow of fraction 200°–210° to a deep red for all fractions above 238°C. Their odor was somewhat sharp and penetrating, suggestive of thymoquinone.

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[18] *Jour. f. prakt. Chem.* II, 3(1871), 54.
[19] *Atti della Reale Accademia dei Lincei Rendiconti* (5) 10, 1(1901) 96.

Several of these red oily products were added to a relatively large volume of water and after saturation with sulphur dioxide the mixture was warmed and violently shaken. After standing several days the color of the oils had changed to a light yellow and a white solid had separated. This was filtered out, recrystallized from boiling water and dried. It melted at 141°–142°C.

In endeavoring to identify the alcohols present, by oxidation and the formation of a semicarbazone from the oxidation product, it was observed that after standing a short time in the presence of semicarbazide hydrochloride the oxidation product from the fraction boiling at 220°–230°C gave a precipitate of a bright yellow color. After recrystallization from methyl alcohol the compound melted at 190°C. The red liquid obtained from several other fractions was treated in the same way. All of them gave this yellow compound. In one case the melting point of the compound was 191°–192°C. and in another 194°–195°C. Since it was suspected that the yellow compound thus obtained was the semicarbazone of thymoquinone, a small amount of a compound known to be thymoquinone was treated in the usual way with an amount of semicarbazide hydrochloride slightly in excess of the theoretical amount necessary to form the disemicarbazone. The product obtained had the same color and, so far as examined, the same solubilities as the yellow substance obtained from the high boiling fractions of the oil. It melted at about 191°C. After recrystallization from methyl alcohol it melted at 192°–193°C.

In 1873 Sigel[20] found the dimethyl ether of thymohydroquinone in the oil of the root of *Arnica montana* and by oxidizing with chromic acid mixture the fraction boiling at 224°-245°C. obtained thymoquinone.

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[20] *Annalen,* 170, 358–359.

Some of the red oxidation product was heated with a saturated solution of normal potassium sulphite to 60°-70°C. and thoroughly shaken. After standing a short time the oil was completely decolorized and a white substance had separated. This was removed and boiled with hydrochloric acid but no thymohydroquinone was obtained.

According to Carstanajen[21] thymoquinone and normal potassium sulphite yield a potassium sulphonate compound which is decomposed by boiling hydrochloric acid into thymohydroquinone and sulphric acid.

So far the dimethyl ether of thymohydroquinone has been found in only two other oils. In 1873 Sigel[22] reported having identified it in the root oil of *Arnica montana,* about four-fifths of which seemed to consist of this ether. Recently Semmler[23] reported this ether as a constituent of the oil of *Eupatorium triplinerve* (Ayapana oil), apparently constituting about three fourths of the oil.

IDENTIFICATION OF ACIDS

EXPERIMENT NO. 1.

The alkaline aqueous solution resulting from the saponification of two liters of oil was shaken out with ether in order to remove the small amount of non-saponifiable oil present, then concentrated to a small volume, made acid with sulphuric acid and subjected to steam distillation, the process being continued until practically all the volatile acids had been driven over. The distillate was collected in five fractions, of which the first three, especially, possessed an odor suggesting one or more fatty acids, possibly caproic, caprylic or capric acid, or a mixture of these. All the fractions were thoroughly shaken with an excess of barium carbonate, the latter removed, and silver nitrate solution added to the filtrate as long as a precipitate was formed. The silver salts were filtered out, washed and dried at 100°C. The silver salt from the first fractions darkened considerably on drying, the color diminishing gradually from fraction 1 to fraction 5.

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[21] *Jour. f. prakt. Chem.* II, 15, 480.

[22] *Annalen,* 170, 358-359.

[23] *Ber.* 41. 509-512.

ANALYSIS OF THE SILVER SALTS

Fraction 1. 0.1217gm. of the silver salt left on ignition 0.0643 gm. of metallic silver, corresponding to 52.83% of silver.

Fraction 2. 0.2879gm. of the silver salt left on ignition 0.1685gm. of metallic silver, corresponding to 58.52% of silver.

Fraction 3. 0.2514gm. of the silver salt left on ignition 0.1597gm. of metallic silver, corresponding to 63.52% of silver.

Fraction 4. 0.4014gm. of the silver salt gave by ignition 0.2586gm. of metallic silver, corresponding to 64.42% of silver.

Fraction 5. 0.2643gm. of the silver salt gave on ignition 0.1706 gm. of metallic silver, corresponding to 64.54% of silver.

Silver salt of acetic acid contains 64.64% of silver.

Silver salt of butyric acid contains 55.34% of silver.

Silver salt of valerianic acid contains 51.64% of silver.

Silver salt of caproic acid contains 48.39% of silver.

Silver salt of caprylic acid contains 42.59% of silver.

Silver salt of capric acid contains 38.67% of silver.

From the analytical data obtained it follows that the acid present in fractions No. 4 and No. 5 was almost pure acetic acid, and that in fraction No. 3 acetic acid largely predominated. The presence of acetic acid in fractions No. 4 and No. 5 was further proved by the fact that when small amounts of the silver salt from these fractions were heated with a little ethyl alcohol and a little sulphuric acid the odor of ethyl acetate was developed.

The percentages of silver obtained in the case of fractions No. 1 and No. 2 show there was certainly at least one other acid besides acetic acid present in the original mixture, and in fact one having a higher molecular weight than that of acetic acid. But so far as the analytical results obtained are concerned it cannot be stated definitely what other acid or acids may have been present.

EXPERIMENT NO. 2

The aqueous alkaline liquid resulting from the saponification of another sample of the oil was distilled with steam to remove unchanged oil; enough dilute sulphuric acid was then added to neutralize the KOH present and liberate a part of the fatty acid. This mixture was then shaken out with ether, and the ethereal solution shaken several times with 5 per cent solution of sodium carbonate. In this way the fatty acid was separated from the small amount of phenol which may have been liberated at the same time. The sodium carbonate solution was then made acid with dilute sulphuric acid and the liquid distilled with steam, the distillate being collected in six fractions.

Fraction No. 1 consisted of a turbid liquid with a small amount of a slightly yellowish oily liquid floating on top. The odor was somewhat like that of caproic acid. The oily layer was separated and converted into the barium salt from which the silver salt was prepared. Of the dried salt there was only 0.0669gm. On ignition this yielded 0.0275gm. of metallic silver, corresponding 41.1 per cent of silver. This result would indicate the presence of capric acid mixed with a small amount of some lower fatty acid.

The aqueous portion of distillate No. 1 was treated with barium carbonate, filtered, and from the filtrate the silver salt prepared. 0.1103gm. of salt dried at about 100°C gave on ignition 0.0563gm. of metallic silver corresponding to 51.04 per cent of silver. This result agrees fairly well with the theoretical amount of silver in the silver salt of valerianic acid, though the same result might be obtained from a mixture of lower and higher fatty acids.

From the remaining fractions of distillate almost no silver compound could be prepared.

The liquid which had been partially acidified with sulphuric acid and shaken out with ether was now made slightly acid with dilute sulphuric acid and distilled with steam. Five fractions of distillate were obtained, each having a decidedly acid reaction.

Fraction No. 1. 0.1601gm. of silver salt prepared from this fraction gave on ignition 0.083gm. of metallic silver, corresponding to 51.84 per cent of silver.

Fraction No. 2. 0.1601gm. of silver salt gave on ignition 0.0778gm. of metallic silver, corresponding to 64.24 per cent of silver.

Fraction No. 5. 0.1062gm. of silver salt gave 0.0698gm. of metallic silver, corresponding to 65.72 per cent of silver.

The non volatile acids were not identified.

EUPATORIUM PURPUREUM

This plant, which is most commonly known as Queen of the Meadow, Joe-Pye Weed, Gravel Root, etc., grows quite widely distributed throughout North America. It is one of the largest species of the genus, sometimes growing 8 or 9 feet high. Its flowers are purple, pink, or sometimes nearly white. Its leaves are arranged in whorls of 3 to 6.

As a popular remedy it has been held in high esteem for many years and was accorded official recognition by the United States *Pharmacopoeia* of 1830, New York edition. It still seems to be considered a valuable remedy by physicians of the Eclectic School of medicine. The root is the part used.

To what compound or compounds such medicinal properties as it may possess are due is not known. Although it has been the subject of more or less chemical investigation the only substance which has been studied to any extent is the yellow crystalline neutral principle, *euparin,* discovered by J. U. Lloyd,[24] and further investigated by C. C. Manger.[25]

As the peculiar odor of the flowers suggested the possibility of obtaining from them an interesting volatile oil, about 40 pounds of the fresh material, consisting of leaves and flowering tops were distilled with steam. The material was collected near Madison, on the University Farm.

The distillation was continued about an hour and a half, with the result that no appreciable amount of oil separated from the distillate, which, however, was somewhat turbid and possessed a rather disagreeable odor not unlike that of the flowers.

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[24] *Am. Journ. Pharm.* 1890, 76.

[25] *Ibid.* 1804.

There were indications that the volatile principle is capable of producing decided physiological effects when inhaled.

EUPATORIUM HYSSOPIFOLIUM

This is one of the smallest of the American species of Eupatorium, seldom growing more than three feet high. It is found widely distributed over the eastern part of the United States from Massachusetts to Alabama and Mississippi, growing in dry, sterile soil. It is readily distinguished from all other species of this genus by its opposite, narrowly linear leaves, often crowded in the axils.

In some localities it is considered an antidote to the poisonous bites of reptiles and stings of insects. No chemical examination, it seems, has ever been made of this plant, though its extremely bitter taste suggests the presence of interesting compounds.

In order to learn if it contained volatile oil, about 70 pounds of the herb were subjected to steam distillation. The material was collected near Auburn, Ala., about the middle of September, 1913, and distilled about a month later at the University of Wisconsin.

No oil separated from the distillate.

EUPATORIUM PERFOLIATUM

Of all our native plants this has probably had the most extensive and frequent use as a domestic remedy. Under such names as Boneset, Ague-weed and Feverwort it has been in common use from New Brunswick to Florida, Louisiana, and the Dakotas. The leaves and flowering tops have been official in the *United States Pharmacopoeia* since 1830, but it is rarely prescribed by physicians.

It grows in marshy places on the borders of lakes, ponds, and streams. The stem is from 1 to 5 feet high. The most disstinctive feature of the plant is the character of its leaves, which are connate-perfoliate, each pair resembling a single leaf perforated by the stem.

Although several reports have been made concerning the chemical constituents of this plant little is known with certainty.

M. H. Bickley[26] distilled a small amount of the leaves and flowers but obtained only a "slightly milky odorous distillate". H. B. Parsons[27] made a proximate analysis of the plant and reported among other things traces of volatile oil. Geo. Latin[28] reported a glucoside (eupatorin) and a "small quantity of volatile oil having the disagreeable odor of boiled cabbage." H. F. Kaercher[29] reported finding about 5 per cent of inulin in the root. A complete proximate analysis was made by C. A. Walter[30] in 1900. He reports the important constituents to be (1) a coloring principle, $C_{27}H_{30}O_{17}$, (2) a tannin, $C_{12}H_{18}O_7$, of glucosidal nature, (3) a bitter principle, $C_{35}H_{58}NO_{10}$.

In order to learn definitely how much volatile oil might be obtained from the plant about 30 pounds of the leaves and flowering tops were collected on the University farm and subjected at once to steam distillation. There was obtained a small amount (about 10 minims) of a bluish green oil, lighter than water and of a rather pleasant odor. Judging from this yield it would require about three fourths of a ton of the fresh material to yield one fluid ounce of the oil, though it is quite probable a larger yield would be obtained by cohobating the distillate and working on a larger scale.

THE VOLATILE OIL OF EUPATORIUM SEROTINUM

This plant is indigenous to the eastern part of the United States, its range being from Delaware to Florida, Texas, Kansas and Minnesota. It grows in low alluvial ground, the stem being from three to six feet high. No use seems to have been made of this plant, either in medicine or otherwise.

The material used in the preparation of this volatile oil was collected near Auburn, Ala., about the middle of September 1913. After being dried it was shipped to Madison, Wis., where, about a month later, it was distilled with steam. The weight of the crude material in the fresh condition was about 55 pounds. Practically the whole plant above ground was collected while in blossom, the flowers being apparently the only part of the plant possessing aromatic properties.

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[26] *Am. Jour. Pharm.* 26, 495.
[27] *Am. Jour. Pharm.* 1879, 342.
[28] *Am. Jour. Pharm.* 1880, 394.
[29] *Am. Jour. Pharm.* 1892, 511.
[30] *Proceedings A. Ph. A.* 1900, 216–232.

The oil is unusually difficult to separate, which is shown by that fact that it required about 40 hours of continuous distillation to exhaust the material. The distillate was cohobated, but only a comparatively small amount of oil was obtained. The total amount of oil separated was 128 gm. or about 0.51 per cent based upon the weight of undried material.

PHYSICAL PROPERTIES OF THE OIL

When first distilled the oil was colorless, but upon exposure to air and light soon became highly colored reddish brown. The odor was very similar to that of the flowers, the taste slightly warm and bitterish.

One cubic centimeter of the oil became turbid by the addition of two or three drops of 90 per cent alcohol. By the further addition of about 0.5 c. c. of 90 per cent alcohol the mixture became clear. A further addition of 1.7 c. c. of 90 per cent alcohol caused the mixture to become turbid again. The turbidity was again removed by the further addition of 1.8 c. c. of 90 per cent of alcohol. 1 c. c. of the oil, mixed with 100 c. c. of 70 per cent alcohol formed a liquid which was still slightly turbid. The mixture of 1 c. c. of the oil and 32 c. c. of 80 per cent alcohol was still somewhat turbid.

The specific gravity of the oil at 25°C. with water at 15°C. as the standard was 0.9075. The optical rotation could not be taken directly because of the high degree of color of the oil. To obtain an approximate valuation of the effect on the plane of polarized light one volume of the oil was dissolved in four volumes of 95 per cent alcohol. This solution of the oil showed a levorotation of 7.36° in a 100 mm. tube. The index of refraction was 1.4990 at 24°C. The specific refraction is 0.323.

CHEMICAL CONSTANTS OF THE OIL

The following data were obtained: acid number, 0.508; saponification number, 28.7; saponification number after acetylation, 61.92. On account of the small amount of material at hand the identification of the acid and the alcohol was not undertaken.

TEST FOR PHENOL

Five c. c. of the oil shaken with 4 per cent aqueous solution of caustic potash diminished about 0.2 c. c. in volume, corresponding to about 4 per cent by volume of phenol. The oil emulsified very readily and the emulsion separated very slowly. A sharp line between the oily layer and the aqueous alkaline layer could not be obtained, but the minimum amount of diminution could safely be put at 0.2 c. c.

With choloform and KOH two or three drops of the oil gave a distinct pink color after standing a few minutes, a good indication of the presence of thymol or carvacrol or both. However, there seems to be no record of an oil from the family *Compositae* which contains either of these phenols. Whether the presence of this phenol is due to an impurity or not will have to be ascertained by the distillation and testing of other oils.

The phenol was removed from the total amount of oil by shaking with 4 per cent aqueous KOH, acidifying and extracting with ether. After evaporation of the ether there remained a reddish-brown mixture, having a bitterish pungent taste. With ferric chloride solution this residue gave a purple color, indicating the presence of salicyclic acid.

SAPONIFICATION AND FRACTIONATION OF THE OIL

The oil from which the phenol had been removed was next boiled on a water bath with an excess of alcoholic KOH for three quarters of an hour. The greater portion of the alcohol was then distilled off on a water bath and the alcoholic distillate added to a large volume of water. A very turbid mixture was obtained from which there separated very slowly a few c. c. of an oil having a slight odor of the original oil and also an odor suggesting pinene.

The alkaline liquid remaining in the flask after distilling off the alcohol was mixed with a relatively large volume of water, the oil which separated was removed and washed with water until free from alkali. It was then distilled with steam and collected in five fractions.

The physical constants of these fractions were as follows:

No. of Fraction.	$d \frac{25^\circ}{15^\circ}$	$^{n}D_{20^\circ}$.	α_D for 100 mm. tube.	$\frac{n^2-1}{n^2+2} \cdot \frac{1}{d}$
1	0.9089	1.4992	—37.05	0.323
2	....	1.5010	—31.85	....
3	0.9110	1.5014	—31.07	0.323
4	....	1.5019	—24.85	....
5	0.9196	1.5025	—19.85	0.321

DISTILLATION UNDER ATMOSPHERIC PRESSURE

A few c. c. each of fractions I, II, and V were distilled under ordinary pressure. The greater part of each fraction distilled as follows:

Fraction I between 240° and 275°C.
Fraction II between 250° and 280°C.
Fraction V between 255° and 280°C.

In all cases there was some decomposition and the distillate from each fraction possessed an empyreumatic odor.

The specific gravity, the index of refraction and the boiling temperature indicate that the oil is composed largely of one or more sesquiterpenes, and since the boiling temperature is not constant it is evidently a mixture.

If they were sesquiterpenes of the specific gravity indicated in the above table, fractions I, III, and V would have the molecular refractions 65.982, 65.892, and 65.484 respectively and according to both their specific gravities and their molecular refractions they would belong to the bicyclic sesquiterpenes with two double bonds as shown by the following table given in *G. H. K.* Vol. I, page 327.

	Mol. Refrac. (Calc.)	d_{15°
Aliphatic Sesquiterpenes	69.50	about 0.86
Monocyclic Sesquiterpenes	67.76	about 0.875—0.890
Bicyclic Sesquiterpenes	66.15	about 0.900—0.920
Tricyclic Sesquiterpenes	64.45	about 0.930—0.940

Fraction No. 1 was treated according to the method given in *G. H. K.* vol. 1,334, for the preparation of caryophyllene nitrosite but the result was negative.

A CHEMICAL STUDY OF WISCONSIN WORMWOOD OIL

Although wormwood has been distilled in Wisconsin for more than half a century, the oil produced in this state has never been subjected to a systematic control. Hence, it is impossible at the present time to state within what limits the physical and chemical constants of the Wisconsin oil may be expected to fluctuate. Neither is it known what allowances should be made for slight admixtures of other volatile oil producing plants in the still when a fair degree of care is exercised in the elimination of weeds. The same ignorance prevails with regard to the influences exercised by climatic conditions and methods of cultivation, the degree of development attained by the plant at the time it is harvested, the treatment which the plant receives between cutting and distillation, the length of distillation, the re-use of the aqueous distillate, the effect of the destruction of leaves by insects, etc.

It will require years of careful study to find satisfactory answers to some of these problems. When once found, it should be possible to give material aid to those engaged in this industry and to make the Wisconsin oil the best in the market. Already it would seem that a partial answer at least can be given as to the better methods of cultivation. It appears that the cultivation in rows yields a better oil as well as a better herb than the meadow cultivation in which cattle are permitted to do such weeding as they will. Whether the cultivation in rows will prove equally profitable remains to be seen.

In order to secure the necessary data that might enable the Station to answer questions in the future with regard to perplexing problems, it seemed highly desirable to begin at once with the investigation of samples of Wisconsin oils distilled during the season of 1913. For this purpose the farms in Sauk county that are at present engaged in the raising of wormwood and the distillation of the oil were re-visited by two members of the Station and arrangements were made for procuring average one pound samples of the 1913 distillate. These are numbered 1, 2, and 5 in the list given below. Samples 3 and 4 consisted approximately of one-half pound each and were brought to the Station by Mr. Leander Drew for the purpose of having them compared. No. 6 is the oil distilled by Mr. G. A. Russell, Government Expert at the Northern Station for the Cultivation of Medicinal Plants, a co-operative experiment between the U. S. Department of Agriculture and the University of Wisconsin.

Inasmuch as the wormwood industry is without doubt the oldest medicinal plant industry in the state, and, moreover, one that has proven its capacity to exist, no further justification is required for giving special attention to it at the very beginning of the Station's activity. It is to be hoped that the investigation begun may be continued uninterruptedly for a number of years, for the results of a series of years will be necessary in order to secure the data that are needed for a better understanding of the subject.

SAMPLES OF 1913 OIL

No. 1. One lb. of oil distilled by Harry Drew, Sauk Co.
No. 2. One lb. of oil distilled by Gannon, Sauk Co.
No. 3. One-half lb. of oil submitted by Leander Drew, Sauk Co.
No. 4. One-half lb. of oil submitted by Leander Drew, Sauk Co.
No. 5. One-half lb. of oil distilled by Henry Haggard, Sauk Co.
No. 6. Oil distilled by G. A. Russel on the Northern Station, Madison, Dane Co.

ODOR AND COLOR

In odor and color these oils show very little difference, number six probably having the most pleasant odor. The color of all the samples was a very deep brown. It was, therefore, impossible to determine the optical rotation.

On exposure to the air in thin layers these oils soon became greenish-blue and finally deep blue. From observations made when the oils were rectified by steam distillation it is concluded that the blue compound results from the high boiling constituents of the oil. Light does not seem to have any influence in the formation of this blue compound.

SPECIFIC GRAVITY

The specific gravity of each sample was determined by means of the pycnometer and that of five samples also by means of the Mohr-Westphal Hydrostatic balance with the following results:

Sample of Oil	$d\frac{25^\circ}{25^\circ}$ by pycnometer	$d\frac{25^\circ}{15^\circ}$ by hydrostatic balance
1	0.9350	0.9335
2	0.9230	0.9215
3	0.9350	0.9340
4	0.9231	....
5	0 9263	0.9225
6	0.9364	0.9355

The specific gravity given in Gildemeister and Hoffmann, *The Volatile Oils,* is from 0.9250 to 0.9550. From the preceding data it will be seen that samples No. 2 and 4 are unusually low in specifiic gravity.

INDEX OF REFRACTION

The index of refraction was determined by means of the Abbé Refractometer at the temperature of 19°C.

No. of samples.	Dn_{19°
1	1.4712
2	1.4705
3	1.4712
4	1.4675
5	1.4721
6	1.4725

SOLUBILITY IN 80 P. C. ALCOHOL

The high degree of color makes it somewhat difficult to determine the solubility of these oils accurately. The solubility of all these samples seemed to be practically the same, one c. c. of each requiring between 0.7 c. c. and 0.8 c. c. of 80 p. c. alcohol to form a clear liquid. Gildemeister and Hoffmann state that the oil forms a clear solution with 2 to 4 parts of 80 p. c. alcohol.

SAPONIFICATION OF THE OILS

Two determinations were made in each case. Between four and six grams of the oil were heated on a boiling water bath with 50 c. c. of an approximately semi-normal alcoholic potassium hydroxide solution. The time of heating was one half hour and one hour respectively. The alkaline mixture was then diluted with distilled water so that the aqueous portion would measure 500 c. c. This solution was then titrated in 100 c. c. portions, using approximately semi-normal sulphuric acid. Phenolphthalein was used as indicator. The solutions were yellowish to yellowish-brown in color. In some cases the solution from the mixture which had been heated a half hour was darker than that from the mixture which had been heated an hour although the conditions of heating were apparently the same. The 100 c. c. portions of solutions were placed side by side on a white background and acid run in until the color was of the same shade as that of a portion of the solution to which no indicator had been added. Usually a small drop of the acid was sufficient to remove the pink color. This solution was then used as a color standard in titrating the last portion. The results are given in the following table:

Sample of oil	Gms. of oil used	C.C. of $\frac{N}{2}$ alc. KOH used	Length of time heated	C. C. $\frac{N}{2}$ H_2SO_4 required for 100 c.c. of solution	Saponification number	Amount of thujyl alcohol	Amount of ester expressed as thujyl acetate
1 a	4.7376	56.7	half hour	7.94	100.4	27.61	35.14
1 b	5.2484	56.7	one "	7.6	99.7	27.42	34.89
2 a	5.3329	56.7	half "	8.45	75.8	20.84	26.53
2 b	5.4642	56.7	one "	8.46	73.78	20.3	25.83
3 a	5.1840	56.7	half "	7.63	100.19	27.55	35.07
3 b	5.3092	56.7	one "	7.64	97.56	26.84	34.16
4 a	5.2851	56.47	half "	7.61	97.58	26.84	34.16
4 b	4.9747	56.62	one '	7.85	97.65	26.85	34.18
5 a	5.6123	56.81	half "	7.5	96.29	26.48	33.70
5 b	5.6400	56.81	one "	7.56	94.32	25.93	33.00
6 a	5.1156	56.81	half "	8.08	89.61	24.64	31.36
6 b	5.5468	56.81	one "	7.6	94.9	26.10	33.21

RECTIFICATION OF THE OILS

100 c. c. each of samples Nos. 1, 2, 3, and 6 were subjected to steam distillation. From No. 1 about 95 c. c. of oil were recovered. 94 c. c. were obtained from each of Nos. 2 and 3. From No. 6 a smaller amount of oil was obtained, namely 88 c. c. In each case the distillation was continued until practically no oil separated from the distillate. The color of the first few cubic centimeters of oil carried over in each case was very light brown but as the distillation proceeded the color deepened so that the color of the rectified oil was only slightly less pronounced than that of the original oil. In each case the last portion of oil which passed over was very highly colored—almost black. A drop of this on exposure to the air soon became blue.

SPECIFIC GRAVITY OF THE RECTIFIED OILS

The specific gravity was determined by means of the Mohr-Westphal Hydrostatic balance, the temperature of the oils being

25° C. For the purpose of comparison the sp. gr. of the original oils and of the corresponding rectified oils is given in the following table.

Sample of oil	Original oil	Rectified oil.
1	0.9335	0.9312
2	0.9215	0.9190
3	0.9340	0.9303
6	0.9355	0.9200

SAPONIFICATION OF THE RECTIFIED OILS

The same process was used here as in the saponification of the original oils. One determination was made in each case and the length of time of heating was a half-hour. The following saponification numbers were obtained. For the sake of ready comparison, the saponification values of the original oils are included in the tabulation.

Sap. No. of rectif. oil	Sap. No. of orig. oil
Sample No. 1.—105.8	100.4
Sample No. 2.—79.11	75.8
Sample No. 3.—98.97	100.19
Sample No. 6.—88.57	89.61

ACETYLATION OF THE OILS

10 c. c. of each sample of oil was acetylized according to the directions given in Gildemeister and Hoffmann, *The Volatile Oils*, p. 195. The length of time of heating was one hour.

SAPONIFICATION OF THE ACETYLATED OILS

The same procedure was followed here as previously described except that 100 c. c. of the alcoholic potassium hydroxide solution were used for each determination. The length of time of heating was in each case one hour. The saponification numbers, the corresponding amount of alcohol as $C_{10}H_{18}O$, the amount of combined alcohol present as acetate, the amount of free alcohol in the oils, and the amount of acetate present are given in the following table:

Sample of oil.	Saponification number.	Corresponding amount of alcohol.	Alcohol combined as acetate.	Amount of free alcohol in oil=thujyl alc.	Amount of acetate present=thujyl acetete
		Per cent.	Per cent.	Per cent.	Per cent.
1	157.13	48.97	27.42	21.55	34.89
2.............	113.93	34.25	20.30	13.95	28.83
3.............	134.29	41.07	26.84	14.23	34.16
4.............	118.44	35.74	26.85	8.89	34.17
5.............	129.53	39.45	25.93	13.52	33.00
6.............	125.41	38.06	26.10	11.96	33.12

FRACTIONATION OF THE OILS

Sample No. 1. The distillation was carried out in a Ladenburg flask, at ordinary pressure and over a bare flame. The amount of oil used was 50 c. c. The rate of distillation was about 60 drops per minute. The distillate was collected in fractions of five cubic centimeters each. In the case of this oil a small amount of liquid, probably 0.5 c. c., came over near 100°C but the mercury rose rapidly to about 195°. Eight fractions were collected. The first fraction was of a light yellowish brown color the intensity of color being too great to permit taking the optical rotation with any degree of accuracy. It was seen, however, to be dextrorotatory. About 0.5 c. c., dissolved in 3.5 c. c. of 95 p. c. alcohol, gave a rotation in a 50 mm. tube of about +3.1°. Fraction No. 2 was of about the same shade of color as fraction No. 1, but the highest fractions were quite highly colored. The temperature at which the fractions came over was as follows:

Fraction No. 1	195°–203°C
Fraction No. 2	203°–206°C
Fraction No. 3	206°–207°C
Fraction No. 4	207°–208°C
Fraction No. 5	208°–210°C
Fraction No. 6	210°–214°C
Fraction No. 7	214°–219°C
Fraction No. 8	219°–232°C

After standing 24 hours in a tightly stoppered vial, fraction No. 2 had become light greenish in color. The other fractions appeared not to have changed in color. After standing several days in small stoppered vials all the fractions had become greenish blue, the depth of blue gradually increasing with increase in boiling point.

Sample No. 2. In this case there appeared to be more water present. Quite a number of drops of water condensed in the neck of the flask. Practically no liquid passed over below 190°. Most of the first fraction came over between 195° and 202°. The appearance of the fractions was just like that of the corresponding fractions from oil No. 1. The temperature at which the fractions distilled was as follows:

Fraction No. 1	195°–202°
Fraction No. 2	202°–205°
Fraction No. 3	205°–207°
Fraction No. 4	207°–210°
Fraction No. 5	210°–213°
Fraction No. 6	213°–217°
Fraction No. 7	217°–223°
Fraction No. 8	223°–243°

After standing 24 hours in a small stoppered vial fractions 2 and 3 had changed to a light green color. After standing several days these fractions were of about the same color as the corresponding fractions from sample No. 1.

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SAW PALMETTO

A PHYTOCHEMICAL STUDY OF THE FRUIT OF SABAL SERRULATA

BY

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A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
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SYNONOMY*

The Index Kewensis, vol. 4, pp. 772 and 884 refers to Bentham and Hooker, *Genera Plantarum* where in vol. III, pp. 926 and 1228, the following information is found: The original genus *Sabal* was changed to *Serenaea* by Hooker and again changed to *Serenoa* by Hooker fils. The following species names are recorded;

Serenoa Serrulata[1]. (Hook.)
Sabal Serrulata[2]. (Roem. and Schult.) Hook. f.
Diglossophyllum[3]. (H. Wendl.)

The following common names are in use more or less;

Saw palmetto[4].
Cabbage palm[5].
Cabbage palmetto[6]. (Sabal palmetto)
Palmetto scrub[7].
Palmetto[8].
Scrub palm.[8]

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* The older literature on the subject is very confusing. Thus Porcher, *Resources of the Southern Fields and Forests* (1863), pp. 525 to 527 distinguishes between the Saw Palmetto (*Chamaerops serrulata L.*), the tall palmetto (*C. Palmetto*, Mich.) and the dwarf palmetto (*Sabal adansonii*, Guerns). It is under the "tall palmetto" that he makes mention of the use of the fruit as food for Indians and hunters, also of the use made of the stems for scrubbing brushes. In this connection compare also C. S. Sherrard (1894).

[1] The only authors, included in the appended bibliography, who refer to the plant by this name are Schnitzer (1895) and Trimble (1896).

[2] Referred to by this name by J. Moeller (1883), C. C. Sherrard (1894) and F. A. Sieker (1895).

[3] C. A. S. (1892) refers to the plant as *Sabiana serrulata*, presumably a printer's or typographical error.

[4] The following authors included in the appended bibliography, refer to the plant by this name: J. B. Read (1879), C. A. S. (1892), J. M. Dixon (1894), C. C. Sherrard (1894), Rusby, Bastedo, Coblentz (1895), Sherman & Briggs (1899), O. Schreiner (1900), Consular Report (1901).

[5] The large terminal leaf buds are used as vegetable particularly by the "negroes who are credited with a special fondness for cabbages which can be had without agricultural forethought or labor." The removal of the bud kills the young tree which yields the most succulent ones. (Sargent, 1896).

[6] Sargent (1896).

[7] *Am. Disp.* 18th ed. p. 1751.

[8] Trimble (1896).

NATURAL HISTORY

According to Sargent, this palm which is the most northern arborescent palm in the world, is the best known of the tree palms of the United States. It is indigenous to the coast region of the south eastern states where "probably nothing so delights and instructs northern travellers in the south as their first introduction to a grove of these plants." In his interesting paper, on "*The tree palms of the United States,*" Sargent gives a brief account of the use made of the terminal bud as vegetable and of the fibres of the sheaths of the young leaves in the scrubbing brush industry. He also records a bit of history in relating how the defenses of Charleston harbor behind "a rude stockade made of the stems of the Palmetto" caused this palm to be given a place in the state seal of South Carolina. But he does not say anything about the fruit or its uses. (1896)

While "parts of the plant have been employed in various economic ways" in addition to those mentioned above, *viz.:* "such as the thatching of huts, making of mattresses, straw hats, and paper" (*Am. Disp.*) and suggestions have been made for using the tannic acid of the stems and roots for tanning purposes, it is the fruit which is at present of greatest interest chemically.

"The fruit though sweet and edible, is not regarded as particularly palatable. It is the medicinal part. Animals show a partiality for it, and are said to become fat and sleek when feeding upon the berries." (*Am. Disp.*, ed. 18 (1900) p. 1750.)

The berries have acquired special interest as one of America's contributions to materia medica. Whatever we know about their chemistry has been studied in connection with the manufacture of pharmaceutical preparations. The principal contribution on the subject is that by Sherman and Briggs who made a careful study of the fatty acids found in both pulp and seed. Little more is known about the chemistry of the fruit or, barring Trimble's preliminary research of the tannin, about the chemistry of the entire plant.

As to the medicinal uses of the berries and the preparations made therefrom, it will suffice to refer those seeking information to any one of the standard dispensatories. Exact information as to the physiological action appears to be about as meagre as that available on the chemical constituents, or even more so.

The medical and pharmaceutical interest, which the therapeutic use of the berries has stimulated, has found expression in several accounts. Of these the following may be mentioned.

E. M. Hale, *Saw Palmetto.*—1898.
P. D. & Co., *Pharmacology of the newer materia medica,* pp. 1141 and 1142. Reprint No. 52.
Rusby, Bastedo and Coblentz, *The Pharmacology of Saw Palmetto.*—1895.

THE MATERIAL

The saw palmetto berries, used in the experiments which are recorded in the following pages, were obtained from Florida through the kindness of Professor J. U. Lloyd, to whom thanks are herewith extended for having made possible the continuation of this investigation.

I. The first lot of berries was received in good condition November 21, 1911. After having taken out 100 gm. samples desired for immediate work, the bulk of the berries were preserved in the following manner:

About one-third was covered with a saturated solution of sodium chloride.

About one-third was covered with choloroform water. When the jar was opened in February 1912, some scum had collected at the surface, but the berries appeared to be in perfect condition.

The last third was covered with alcohol. The strong odor of esters of fatty acids was soon noticeable and oily drops rose to the surface.

II. Another lot of fresh saw palmetto berries was received November 9, 1912. The berries which were in excellent condition were kept in two bottles, one having a ground glass stopper, the other a cork stopper. After a short period the disagreeable odor of the berries changed in part to the sweeter odor of esters. As no preserving material had been added it seemed that, if esters were present, the alcohol must have formed as a result of the standing. This material was later examined for alcohol. The berries in the cork-stoppered bottle soon showed signs of mold and after standing over a year they were found to contain worms. This material was used in part for the extraction of possible alkaloid and glucoside.

III. A third shipment of berries was received in January, 1913. These were dried, having been dried according to the usual method employed by Lloyd Brothers.[9] Ten pounds of the fresh berries were reduced to six pounds after drying. The strong odor of the fresh berries had almost completely disappeared.

IV. A fourth lot of berries was obtained in December, 1913. As the saw palmetto berries come from Florida, the long period of shipment, it was thought, might cause considerable change in the berries. It was, therefore, regarded desirable to send preserving liquids to the collectors thus protecting the fresh fruit from outside influences. Through the kind efforts of J. U. Lloyd the material was supplied by the Florida Botanical Drug Co., of Jacksonville, Fla., who sent a special collector to secure fresh berries of the desired quality. Hence the bottles containing the preserving liquids were sent to Florida and the freshly picked berries were placed in these bottles. The following bottles were received in excellent condition.

12 containing berries alone.
6 containing berries in alcohol.
6 containing berries in toluene.
4 containing berries in brine.
4 containing berries in water saturated with xylene.
4 containing berries in water saturated with chloroform.

The toluene in which some of the berries had been preserved showed a fluorescence. The berries kept under toluene seemed to lose part of their moisture which sank to the bottom of the container. This was also true of the berries which were not covered with any preserving liquid.

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[9] Personal communication, letter of Jan. 7, 1913, by J. U. Lloyd to E. Kremers.

THE CHEMISTRY OF SAW PALMETTO

The immediate cause for the investigation here recorded will be found in the mystery that surrounds the presence of a so-called volatile oil in some fresh berries, more particularly those preserved in alcohol, and the absence of such a substance in the drug, that is, in the dry berries. A preliminary investigation was undertaken in this laboratory by O. Schreiner in 1900. After a careful examination of the records and some preliminary experimentation he arrived at the following conclusion:

"The above result clearly shows that the volatile oil as such is certainly not present in the dried berries. Whether or not it is present in the fresh, recent fruit, or whether it is formed by the slow action of the fatty acids on the alcohol in which the berries are kept, can only be decided by experiment. Prof. Lloyd has kindly offered to subject some of the fresh, unpreserved fruit to distillation as soon as the crop is ripe."

It is through the co-operation of Professor Lloyd that it has been possible to solve the question as to the pre-existence or formation of the volatile oil. Not only did he distill fresh berries as promised, but he also subjected, upon request, fresh berries to the influence of alcohol for a period of ten years and then generously contributed the so-called volatile oil which had been formed. Thus it became possible to resume the work on a more satisfactory basis. The record of the experiments bearing directly upon this aspect of the chemistry of the saw palmetto will be found under the heading "Volatile Oil."

The recent work that has been done on ester-forming enzymes naturally created the desire to ascertain what influence, if any, the enzymes present in the berries exerted on the formation of the esters found in the volatile oil artificially produced on a relatively large scale by storing the fresh berries in alcohol, or on a minute scale by alcoholic fermentation of the fresh berries when not preserved in alcohol.

The study of possible ester formation in plants has been pursued in this laboratory along several lines. Thus the rate of addition of organic acids to unsaturated hydrocarbons with the formation of esters has been studied in several directions[10]. The rate of esterification of menthol and menthone in the presence of acetic acid has been partially studied by the writer[11]. The rate of esterification of the fatty acids found in the saw palmetto berries, with ethyl alcohol was made the subject of a special investigation and has demonstrated that enzymes are not necessary to the formation of ethyl esters of the fatty acids in the berries preserved in alcohol.

The contrast between the fresh and the dried berries, both of which appear to have been used for the manufacture of galenical preparations, invited a comparative study. This led first of all to the study of the moisture content of the fresh berries. It thus became apparent at once that the ordinary methods could not be applied because of the volatility of the free acids. The application of the xylene method then led to the observation that under the conditions of this experiment, the xylene vapors carry over not only the moisture and the free acids in the pulp but basic substances as well.

Thus the investigation which was begun with the object in view of solving the mystery of the formation of a volatile oil consisting entirely of ethyl esters of fatty acids resolved itself into a general chemical study of the saw palmetto fruit. The results of this investigation are here recorded.

The scope of this chemical study, so far as time and material permitted, is indicated in the table of contents.

MOISTURE

The moisture content of the saw palmetto berry is a matter of general interest and hence worth determining. However, the moisture determination in this instance is also of special interest for two reasons. First of all, the question arises, to what extent do the volatile fatty acids interfere with the conventional methods of moisture determination as applied to plants or parts of plants. Second, an approximate determination of the moisture content of the fresh berries is of particular interest because these berries are not infrequently preserved in alcohol. As will be shown later, the formation of the so-called volatile oil of saw palmetto in material thus preserved is due to the condensation of the fatty acids in the berries with the ethyl alcohol in which they have been preserved. Naturally, the rate of condensation as well as the amount of esters formed must depend, in part at least, upon the extent to which the ethyl hydroxide content of the original alcohol used is reduced by the moisture content of the berries. For these two reasons a number of moisture determinations were made according to various methods.

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[10] A. F. Sievers, *The Addition of Organic Acids to Unsaturated Hydrocarbons'* U. W. Bulletin No. 434 (Science Series vol. 4, No. 3, pp. 39 to 80.)

A. DuMez, (Unpublished results) R. Schultz (Unpublished). C. D. Geidel, *A Comparison of Oxygen Conveyance of Phellandrene and Pinene, and the Germicidal Properties of the So-called Peroxides of the Terpenes.* Master's Thesis U. W. 1913.

[11] Chas. Mann, *Esters of Menthol*, A Revision, Master's Thesis U. W. 1911 (unpublished).

Apparently but little previous work has been done on the moisture content of the saw palmetto berry. Sherrard[12] records that the "dry ripe berries" lose 6 per cent at 45°C. and 10.339 per cent at 100°C to 105°C. Trimble[13] determined the moisture content of the stems and roots, but not of the berries. Of the fresh berries no moisture determinations appear to have been made, yet it is the moisture content of these that is of particular interest.

Moisture determinations were made in connection with materials collected in three successive years, also, according to several methods. Soon after their arrival the best berries were selected for this purpose. It was also the endeavor of the operator to handle the different lots as much in the same manner as possible. As an additional precaution relatively large amounts, *viz.:* 75 to 100 gms. were used for each determination, thereby reducing to a minimum errors due to the selection of the fruit and to handling. In the following record of the several experiments the details are reduced to tabular form wherever possible.

A comparison of the results recorded below reveals that, whereas the individual experiments according to the same method and as appplied to the same material agree fairly well, the results of different methods though applied to the same material do not agree as well. This was to be expected for reasons already alluded to. That the different materials should give varying results was also to be expected. Although all of the berries used were fresh, mature berries, there naturally must have been some variation as to maturity in different years. Moreover the time between collection and assay varied more or less in different years. However, the results are sufficiently approximate to admit of their use for the principal purpose for which they have been intended. It should also be stated that extraordinary care was exercised in collecting the material during the fall of 1913.[14]

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[12] *Proc. A. Ph. A.*, 42, p. 311.

[13] *Garden and Forest*, 9, p. 182.

From the point of view of analytical technique, the results of experiments I and II are of special interest. They show that the ordinary moisture determination by difference yields results that may be 6.5 and 7+ per cent out of the way, introducing an error of over 10 p. c. on the moisture content. Experiment II also seems to reveal that the difference between the ordinary drying method and the xylene method is apparently due in small part only to volatile acids, both free and combined. Experiment six, however, reveals the fact that this difference may be much smaller with a given material and that it may be wholly accounted for by the amount of fatty acids, free and combined. Whenever the amount of acids was determined, the computation was made for caprylic acid, the middle member of the mixture of volatile homologous acids found by Sherman and Briggs.

Experiments IV to VII inclusive were performed on the same material, experiments IV and V and VI being started as nearly the same time as practicable, and experiment VII several weeks later.

In connection with this group of experiments it is noteworthy that the average difference between IV and VII is 7 per cent (result No. 1 in Experiment VII is omitted in computing the average for this experiment for the reason stated in the account of the experiment). Hence drying in air at between 105° and 110°C. gave results appreciably higher than drying in an atmosphere of hydrogen between 100° and 105°C. This difference is possibly further accounted for by the fact that the thermometers recorded the temperature of the oven, not necessarily of the substance being heated. No doubt, the current of hydrogen used in experiment seven kept down the temperature of the substance being dried below that recorded by the thermometer in the oven.

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[14] See letter of Nov. 27, 1913 to E. Kremers from Florida Botanical Drug Co., Jacksonville, Fla.

The relatively close agreement between the results in Experiment V (drying in vacuum over potassium hydroxide) and Experiment VI (xylene method) are particularly noteworthy. For practical purposes it would seem that the xylene method yields the most reliable and relatively speedy results. No doubt, this method or some modification thereof will have to be used more and more in phytochemical work, whether investigative or merely analytical.

First Experiment. Three samples of 100 gms. each of material I, were immediately dried (Nov. 22, 1911) on a steam radiator until of constant weight and the loss of weight computed as moisture as is commonly done. The experiment was continued after January 5, 1912 in order to ascertain whether the drying process was followed by any oxygen absorption. The following figures represent the loss in weight, expressed in grams, hence percentage loss.

	A.	B.	C.
Nov. 22, 1911	57.60	57.30	55.60
	58.00	57.70	56.90
	58.60	57.90	57.05
Jan. 5, 1912	59.08	58.15	57.30
Jan. 12, 1912	59.30	58.24	57.53

That the loss was not entirely due to moisture was very apparent during the first few days, when the odor of volatile fatty acids was very perceptible. The slight increase during the period Jan. 5 to Jan. 12, may be explained by assuming that either moisture or oxygen was taken up, or that both were. Inasmuch as the pulp darkens very much when dried in the ordinary atmosphere containing oxygen, whereas it remains light in color when dried in vacuum and in a current of hydrogen, it may be assumed that the absorption of oxygen plays a role of some importance in the ordinary methods of drying.

Second Experiment. In order to make a more accurate moisture determination the xylene method, elaborated by A. L. Dean[15] for the estimation of moisture in creosoted wood, was tried. For this purpose three samples of 100 grams each of the fresh berries of material No. 1 had been preserved under xylene saturated with water. The moisture determinations were made eight weeks later. In order to distill over all of the water, additional moist xylene had to be used. The amount of berries used being so large, it was necessary to use a number of graduated funnels for the collection of the distillate and the measurement of the separated water. The results are herewith recorded:

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[15] Circular No. 134, (1908) Forestry Service, U. S. Dept. of Agr., *The Estimation of Moisture in Creosoted Wood.*

A.	B.	C.
52.12 per cent	52.10 per cent	49.93 per cent

Whereas these results agree very well among themselves, they do not at all agree with the results of the first or conventional method. That volatile fatty acids are computed as moisture according to the first method has already been pointed out. In order to ascertain to what extent these volatile acids or any of their esters might be responsible for this difference of from 6.5 per cent to 7 per cent both the aqueous distillates and the xylene distillates were titrated.

The titration of the xylene distillates, however, did not give sharp end reactions with phenolphthalein, when neutralized with alcoholic potash, hence they were shaken out with aqueous potash and the amount of KOH consumed determined by back titration. Finally, to guard against any possible esters, both aqueous and xylene distillates were saponified with alcoholic potash by heating for one and one-half hours.

The results of these determinations are herewith tabulated. In each case the mixed acids are computed as capryllic acid, $C^8H^{16}O^2$.

Water	A.	B.	C.
Water	Per cent 52.120	Per cent 52.100	Per cent 49.930
Acid in aq. dist., direct titration	0.155	0.135	0.150
Acid in xylene dist., direct titration	0.057	0.047	0.095
Acid in xylene dist., shaken out	0.068	0.0604	0.111
Acid as ester in aq. ist	0.055	0.052	0.088
Acid as ester in xylene washings	0.012	0.111	0.0086
Acid as ester in xylene dist	0.107	0.0946	0.1008
Total water and acid (free and combined) in per cent	52.517	52.452	50.3884

The correction thus made accounts for but a very small part of the difference. The difference due to other volatile products is represented by the following figures: A. 6.783 per cent, B. 6.788 per cent, C. 7.142 per cent.

To what substance or substances this difference may be due has not yet been ascertained. The distillation of fresh saw palmetto berries with xylene on a large scale might lead to some interesting results.

Third Experiment. In order to account for the discrepancies recorded above, the crushed berries (material II) were dried, until of constant weight, in a flask which was heated to a temperature of 110°C. in an electrically heated oven. In order to facilitate the removal of the water, the berries were heated in a current of air and the vapors, after leaving the drying flask, were passed, first through water, then through alcohol, and finally collected in an aspirating bottle. The gases collected in the aspirating bottle were analyzed and found to be of the composition of air. The acid that had collected in the wash bottles was computed as caprylic acid as before, the esters as ethyl caprylate. The results of two experiments, after several preliminary trials, are herewith recorded.

	A.	B.
Weight of fresh berries	114.80 grams	122.44 grams
Weight of dried berries	51.10 "	52.04 "
Percentage loss (Moisture, acids & esters)	55.50	57.50
Acids in water	1.33 per cent	1.47 per cent
Esters in water	0.33 "	0.442 "
Acids in alcohol[16]	1.12 "	1.15 "
Total percentage of acids and esters	2.781	3.062
Computed loss due to moisture	52.719	54.438

Fourth Experiment. For this experiment material IV was used. The skins of the berries were cut loose from the pulp; then the material weighed in Petrie dishes and dried at 110°C. in an electrically heated oven and finally in a gas heated oven until no more loss occurred, but a slight increase in weight manifested itself. When dried in this way the pulp turned from yellow to almost black. Following are the results:

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[16] The esters in the alcohol were not determined owing to the loss of the material by accident.

	A.	B.	C.
Weight of fresh berries Dec. 26	28.4600 grams	25.4400 grams	28.000 grams
" " dried " Dec. 29	8.6789 "	7.3935 "	
" " " " Dec. 30	8.5860 "	7.3130 "	7.5820 "
" " " " Jan. 4	8.6200 "	7.3407 "	7.6049 "
Percentage loss	69.8300	71.2500	72.9200

Fifth Experiment. In this experiment the same material as in experiment four was used. The berries were prepared and weighed out in a similar manner as in the preceding experiment, except that the drying was accomplished by means of a vacuum at room temperature. The desiccating agent was stick caustic soda which was used because it would fix any volatile acids coming from the berries. After the period of drying, the pulp of the berries still maintained most of its original yellow color. The results are herewith recorded.

	A.	B.	C.
Weight of fresh berries Dec. 26	26.849 grams	28.9714 grams	29.770 grams
" " dried " Dec. 29	11.3679 "	13.0684 "	11.9994 "
" " " " Jan. 4	10.4536 "	11.8514 "	11.5674 "
" " " " Jan. 5	10.3872 "	11.7714 "	11.4984 "
" " " " Jan. 9	10.2464 "	11.6014 "	11.3500 "
" " " " Jan. 11	10.2150 "	11.5630 "	11.3156 "
" ". " " Jan. 16	10.1388 "	11.4670 "	11.2333 "
Percentage loss	62.27	60.42	62.23

Sixth Experiment. For this experiment the xylene method as described under experiment No. 2, was used. The berries of material IV were crushed and allowed to stand over moist xylene for two days before distillation. The results are herewith recorded.

	A.	B.	C.
Weight of fresh berries	25.7754 grams	25.2126 grams	22.0256 grams
C. C. of moisture	15.25	15.31	12.54
Percentage moisture	59.16	60.72	56.93
Water layer	59.160 per cent	60.720 per cent	56.930 per cent
Acids in water layer	0.266 " "	0.219 " "	0.287 " "
Esters in water	0.262 " "	0.000 " "	0.324 " "
Acids in xylene layer	0.124 " "	0.169 " "	0.145 " "
Esters in xylene layer	0.225 " "	0.176 " "	0.263 " "
Total loss	60.037 " "	61.284 " "	57.949 " "

Seventh Experiment. In this experiment the berries of material IV were electrically heated in a tube to 105°C. after the skins had been loosened from the pulp. Hydrogen gas, freed from any hydrochloric acid gas by passing through strong potash solution and dried by passing through sulphuric acid, was passed through the tube. The moisture-saturated gas was passed through a chilled tube to condense most of the moisture, then through a small calcium chloride absorption apparatus, then through standard alkali and finally through alcohol. Any free volatile acids or volatile esters were caught in the alkali and alcohol. The heating was continued for four or five days. Following are the results.

	A.	B.	C.
Weight of fresh berries	18.920 grams	18.9947 grams	17.8900 grams
Weight of dried berries	5.8691 "	6.6520 "	6.1109 "
Percentage loss on weight	67.40 per cent	64.97 per cent	65.80 per cent
Moisture found	63.466 " "	61.983 " "	62.949 " "
Acids in moisture	0.350 " "	1.340 " "	0.269 " "
Esters in moisture	0.514 " "	0.167 " "	0.322 " "
Acids in KOH and Alcohol	4.000 " "	0.894 " "	0.604 " "
Esters in KOH and Alcohol	0.235 " "	0.072 " "	0.125 " "
Total loss	68.565 " "	64.456 " "	64.269 " "

In A the hydrogen used was not freed from hydrochloric acid vapors which may account for the high acid content in the KOH alcohol bottles.

Tabulation of Moisture Determinations

In order to make possible a more convenient comparison of results of experiments one to seven, those data that are final in the several experiments are herewith tabulated.

	1911 Material	1912 Material	1913 Material
First Experiment			
Dried on steam radiator. No corrections for fatty acids	A. 59.08 per cent B. 58.15 " " C. 57.30 " "		
Average	58.12 per cent		
Second Experiment			
Xylene Method. Fatty acids, etc. eliminated	A. 52.12 per cent B. 52.10 " " C.* 49.93 " "		
Average	52.11 per cent		
Third Experiment			
Dried in flasks at 105-110° C. Corrections for fatty acids, etc. made		A. 52.72 per cent B. 54.44 " "	
Average		53.58 per cent	
Fourth Experiment			
Dried in Petrie dishes at 105-110° C. No corrections for fatty acids			A. 69.83 per cent B. 71.25 " " C. 72.92 " "
Average			71.33 per cent
Fifth Experiment			
Dried in vacuum at room temperature. No corrections for fatty acids			A. 62.27 per cent B.* 60.42 " " C. 62.23 " "
Average			62.25 per cent
Sixth Experiment			
Xylene method. Fatty acids eliminated			A. 59.16 per cent B. 60.72 " " C.* 56.93 " "
Average			59.94 per cent
Seventh Experiment			
Dried in an atmosphere of hydrogen at 105° C. Corrections for fatty acids made			A.* 63.47 per cent B. 61.98 " " C. 62.95 " "
Average			62.46 per cent

*Eliminated for average.

In a comparison of the above data several important factors should be borne in mind. The material collected in December 1913 was the best of the three lots examined. All of the berries utilized for moisture determinations were sound, hence the pulp had lost little or no water. The xylene method may be regarded as the only one which in this instance yields satisfactory results. Hence, in accordance with the best results available, it may be assumed that the fresh, ripe berries collected in December contain sixty per cent of water.

RATIO OF SKINS, PULP, AND SEEDS AND THEIR RELATIVE MOISTURE CONTENTS

In all of the previous experiments on the moisture content of the berries, the entire fruit was taken as a unit. Inasmuch, however, as this includes such varied parts as skin, pulp, and seed, each of which represents chemical problems of its own, it was thought of sufficient importance to ascertain, with a fair degree of accuracy, the relative proportions of these parts and their separate moisture contents. The parts were separated as carefully as possible and the percentage of each determined without appreciable loss, 29.5264 grams of perfect berries having been selected for this purpose. The moisture content, so called, was determined for each part by drying in vacuum over solid potassa. The results are herewith tabulated for better comparison.

Material IV	Wt. of	Per cent of	Loss on drying as moisture	Per cent loss on drying
Skins	10.4584 grams	35.42 per cent	6.7843 grams	68.87 per cent
Pulp	10.7510 "	36.41 " "	8.6495 "	80.45 " "
Seeds[17]	8.1908 "	27.74 " "	2.8264 "	34.57 " "
Totals	29.4002 grams	99.57 per cent	18.2602 grams	

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[17] Attention should possibly be directed to the fact that the seeds were not comminuted. The same holds true with regard to the conventional methods of drying the entire berries. The process, however, was continued until the seeds were of constant weight.

The total loss of 61.16 per cent "moisture" agrees fairly well with the result obtained for the entire berries, the difference of about one per cent being readily accounted for by loss of water while manipulating the berries.

INORGANIC CONSTITUENTS

C. C. Sherrard[18] in 1892 was the first to report on the ash content of the dry ripe saw palmetto berries, also to record the results of a qualitative analysis thereof.

1. Weight of ash at low red heat	4.142 per cent
2. Ash soluble in water	2.772 " "
3. Ash insoluble in water	1.370 " "
4. Ash soluble in hydrochloric acid	0.714 " "
5. Ash soluble in caustic soda solution	0.515 " "
6. Ash insoluble in above solvents	0.141 " "
7. The water solution, analyzed qualitatively, was found to contain	
a.) Aluminum	trace
b.) Calcium	trace
c.) Magnesium	trace
d.) Potassium	considerable
e.) Sodium	considerable
f.) Chlorides	considerable
g.) Sulphates	trace
h.) Nitrates	trace
i.) Carbonates	considerable
8. Insoluble in water, soluble in hydrochloric acid	
a.) Calcium	trace
b.) Magnesium	considerable
c.) Sulphates..	trace
9. Insoluble silicates	0.141 per cent

According to Bastedo[19] the mesocarp reveals a single row of square or oblong narrow cells which contain calcium oxalate crystals, though sometimes wanting.

ASH DETERMINATIONS

For the following ash determinations, perfect berries from material No. IV were selected, one berry being used for each determination. The skin was cut open and a gentle heat applied at first so as to avoid loss from spattering. Bunsen burner and muffle were used. Finally, the heat was raised to a bright red. The resulting ash had a glassy appearance. The percentage is computed both with reference to the fresh and dry berries.

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[18] *Proc. A. Ph. A.*, 42, p. 309.

[19] H. H. Rusby, W. A. Bastedo, and V. Coblentz, *The Pharmacology of Saw Palmetto*, in *Proc. N. J. Pharm. Assn.*, 25, p. 45.

	A	B
Ash content of the wet berries	0.575 per cent	0.541 per cent
Ash content of the dry[20] berries	1.440 per cent	1.352 per cent

Ash determinations were also made of the seed with the following results obtained:

	A	B
Ash content of the wet seeds	0.865 per cent	0.904 per cent
Ash content of the dry[21] seeds	1.322 per cent	1.381 per cent

These results are but about one-third of those obtained by Sherrard. The supposition, that Sherrard's dry berries were admixed with sand, will not hold since he finds less than 0.2 per cent of "insoluble silicates." The assumption, that the high temperature employed may have driven off volatile constituents of the ash, seemed more probable, since potassium and chlorine are reported as being present in "considerable" quantities. Hence, a second ash determination was made. The material (four berries weighing between 16 and 17 grams) was charred until it no longer gave off fumes and the charred mass burned after lixiviation. The united ashes were heated to 110°C. The results were again computed, with the following results:

	ASH CONTENT COMPUTED WITH REFERENCE TO			
	Wet Berries		Dry Berries	
	A.	B.	A.	B.
Insoluble ash	0.202 per cent	0.203 per cent	0.505 per cent	0.507 per cent
Soluble ash	0.670 " "	0.706 " "	1.675 " "	1.765 " "
Total ash	0.872 per cent	0.909 per cent	2.180 per cent	2.272 per cent

In like manner the ash determination of the seed was repeated with the following results:

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[20] The moisture result from Exp. 6, xylene method, giving 60.00 per cent was used.

[21] The moisture content of the seeds, 34.57 per cent., was used.

	Ash Content Computed With Reference to			
	Wet Seeds		Dry Seeds	
	A.	B.	A.	B.
Insoluble ash	0.463 per cent	0.338 per cent	0.708 per cent	0.516 per cent
Soluble ash	0.547 " "	0.557 " "	0.836 " "	0.851 " "
Total ash	1.010 per cent	0.895 per cent	1.544 per cent	1.367 per cent

The amount of ash in the seed is 27.2 per cent of the total ash of the berry as calculated from the following data: 18.76 grams of fresh berries produced 1.7053 grams of ash. From the ratio of skin, pulp, and seeds of fresh berries we find that 18.76 grams of berries contain 5.204 grams of seeds. 6.1551 grams of seeds gave 0.05508 grams of ash. By proportion the ash in the seeds of 18.76 grams of berries can be found. This weight over the weight of the ash obtained from 18.76 grams of berries gives 27.2 per cent.

THE SO-CALLED VOLATILE OIL

As early as 1879, Read[22] refers to a volatile oil as well as to a fatty oil in connection with his observations on saw palmetto, but did not isolate either.

J. U. Lloyd[23] appears to have been the first to have isolated this so-called volatile oil in 1890, though he did not publish his observations. The material obtained by him at that time was not examined until ten years later by Schreiner[24].

In 1892, Sherrard reports having obtained 0.54 per cent of volatile oil and 12.80 per cent of fixed oil from the chloroformic extract of the dry berries. Presumably the amount of "volatile oil" was computed by difference. None was isolated, hence its properties were not determined.

Coblentz[25] in 1895 mentions having obtained a very small quantity of volatile oil by steam distillation from the air dried berries, also from the benzol extract of the drug, but he also does not describe it.

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[22] According to Read, the expressed juice separates into three layers, one of which he regards erroneously as volatile oil. Compare with Sherrard who finds two fixed oils.

[23] See correspondence between J. U. L. and E. K., Feb. 6, 1900.

[24] *Pharm. Rev.*, 18, p. 217.

[25] See letter to E. K., March 28, 1900.

In 1899, Sherman and Briggs made a detailed chemical study of both the so-called volatile oil and the fatty oil obtained by expression of the pulp of berries marked three-fourths ripe that had been preserved in the customary manner with alcohol. From the expressed product an oily liquid (about 1.5 per cent) was obtained, only a very small amount of which distilled over, at 16 m. m. pressure or less, between 70 and 270°C. This so-called volatile oil consisted to the extent of about 63 per cent of free acids and about 37 per cent of the ethyl esters of these acids. From 500 grams of oil but 32 grams *i. e.* the first fraction, were liquid, the fractions above 165°C. (16 m. m.) were mostly solid.

In 1900 Schreiner examined not only the so-called volatile oils distilled by Lloyd in 1900,[26] but also two oils that had been separated by Lloyd from the fluid extract[27]. These fatty oils contained but very small amounts of substances volatile with water vapor.

In the same year Lloyd distilled two twenty-five pound lots of dry berries, but no volatile oil resulted[28]. After standing for a day the aqueous distillate separated very small amounts of fatty scales (0.026 per cent and 0.012 per cent respectively) which appeared to be some of the higher acids known to exist in the fruits both free and as glycerides.

At the same time Lloyd preserved twenty-five pounds of fresh berries[29] in alcohol and distilled them January 24, 1910, ten years later[30]. This material also was kindly placed at the disposal of this laboratory by Professor Lloyd. As already indicated, it is this material that caused the resumption of the investigation of saw palmetto more than ten years after Schreiner had worked on this subject in this laboratory. A description of this oil and its properties will be given later. Although in 1900, when Schreiner reported on the so-called saw palmetto oil, its formation was correctly interpreted, this interpretation was but a surmise that remained to be proved. The experiment performed by Professor Lloyd seems to remove all doubts on the subject.

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[26] See letter to E. K., March 26.

[27] See letter to E. K., March 12, 1900.

[28] Pharm. Rev., 18, p. 221.; See letter to E. K., March 26, 1900.

[29] See letter to E. K., Jan. 13, 1902.

[30] See letter to E. K., Jan. 5, 1911.

The so-called volatile oil of saw palmetto was the first to be observed in a representative of the palm family. Its composition was carefully ascertained by Sherman and Briggs, but its quasi biochemical aspects were very dubious indeed. These may now be readily interpreted.

According to Sherman and Briggs, the seeds of the saw palmetto contain about 12 per cent of a fatty oil which consists of the glycerides of practically the same fatty acids found in the so-called volatile oil. The pulpy pericarp of the fruit, preserved in alcohol, yielded upon expression about 1.5 per cent of an oil, about 63 per cent of which consisted of free fatty acids and about 37 per cent of ethyl esters of these acids. The distillation conducted by Lloyd in 1900 on a sufficiently large scale revealed that no appreciable amount of ethyl esters are contained in the fresh ripe berries that have not been preserved in alcohol, but that if the distillation with water vapor be carried on for a sufficient length of time, some of the fatty acids, even the solid ones, may be carried over and separated, provided the aqueous distillate be allowed to stand long enough.

Experiments conducted in this laboratory, and to be reported in detail later on, reveal what was to be expected, *viz.*, that the free fatty acids of the pulp combine with the ethyl alcohol, added as a preservative to the berries, to form esters. The ratio of ester to free fatty acid in excess, as observed by Sherman and Briggs, who, however, do not report the time element, is about 1 to 2, thus showing that the amount of ethyl esters is not large. This again is to be expected if one takes into consideration the extent to which the alcohol used as preservative is diluted by the moisture content of the berries previous to the condensation between acid and alcohol to ester and that this dilution increases slightly with the condensation.

That traces of esters may be found, though no alcohol be added to the berries as preservative, can also be readily understood if it is recalled that the berries contain carbohydrates, and that the berries may remain bulked in the fresh condition for appreciable lengths of time before being dried or preserved with alcohol. That traces of ethyl alcohol are formed under such condition has also been demonstrated.

Under the commonly accepted conception of a volatile oil, saw palmetto berries may well be said to contain traces of such. The odor given off by the berries when being dried readily reveals its presence. However, the volatile substances other than water thus observed (see under moisture) are not the products commonly regarded as the volatile oil of saw palmetto (See Gildermeister, *Die Aetherischen Oele*, ed. II, p. 260). These volatile constituents apparently consist of the lower fatty acids found as glycerides in the seeds and may remain largely dissolved in the aqueous distillate. The solid volatile oil obtained by Lloyd in 1910, which separated from the aqueous distillate upon standing for twenty-four hours apparently consisted of the higher fatty acids which in small part were carried over. The ethyl esters which have been described as the volatile oil of saw palmetto do not exist as such in the berries; neither are they formed, as are glucosidal oils, upon hydrolysis of more complex substances; but they are well nigh entirely the product of condensation of the free fatty acids occurring as such in the pulp with the ethyl alcohol added as preservative to berries used in the pharmaceutical industries. Whether such a product should be designated volatile oil of saw palmetto seems doubtful. That the merest traces of such esters may be formed from ethyl alcohol that has not been added but results as a product of fermentation of berries not preserved, has already been pointed out, but no one has as yet obtained these esters thus formed as a volatile oil.

PROPERTIES OF THE VOLATILE OIL

It has already been pointed out that in 1890, at the request of Professor Kremers, Professor J. U. Lloyd secured fifty pounds of fresh berries not preserved in alcohol, distilled one-half of this amount immediately upon receipt, and preserved the remaining half in alcohol. The distillation of the first twenty-five pounds yielded no volatile oil to speak of, but after the aqueous distillate had been allowed to stand for twenty-four hours, a few scaly crystals, presumably higher fatty acids, separated from and floated on the water. The distillation of the second twenty-five pounds, however, ten years later resulted in "fully four fluid ounces."[31] of oil, thus proving conclusively that the fresh berries are practically devoid of ethyl esters and that the so-called volatile oil of the saw palmetto is a product of the interaction of the free fatty acids of the berries and the ethyl alcohol in which they are preserved. The chemical composition of this oil, as separated from the fatty oil, resulting as a by-product in the manufacture of galenicals was reported by Sherman and Briggs in 1899. It remained, however, to determine the physical and chemical constants of this so-called volatile oil.

The oil placed at the disposal of the writer by Professor Lloyd was examined in July 1914. It was a mobile fluid with only a tint of green, and a fruity, oenanthic odor. The constants as ascertained, are herewith recorded: $d_{27^\circ} = 0.8627$; $n_{27^\circ} = 1.4294$; Iodine value = 2.72 and 4.20; Acid Value = 26.6 and 26.6; Ester Value = 226.3 and 224.8; hence, Saponification Value 252.9 and 251.4. A record of the examination of the oil at the time of its receipt shows it then had a "Sp. gr. at 68°F by pycnometer of 0.868; Saponification Value 261 and 262; optically inactive." However, the report is not signed.

Another sample of volatile oil, distilled about 1890 by Professor Lloyd,[32] presumably from alcoholic material, was likewise placed at the writer's disposal. Its constants were likewise determined in July 1914, and found to be $d_{27^\circ} = 0.8627$; $n_{27^\circ} = 1.4304$; Iodine Value = 3.95 and 4.34; Acid Value = 39.1 and 38.6; Ester Value = 213.3 and 214.8; hence Saponification Value of 252.4 and 253.4.

A comparison of the two sets of constants reveals a striking similarity of the two volatile oils. The iodine value, though small, seems to indicate that some of the oleic acid, as well as the saturated fatty acids, enter into the composition of the oil. Attempts to translate the acid and ester values into percentages did not prove satisfactory. As is known from the work of Sherman and Briggs, the mixture of fatty acids is fairly complex, ranging from an acid with six carbon atoms to one with sixteen carbon atoms. In the moisture determinations, corrections for volatile acids were made by the arbitrary use of the molecular weight of caprylic acid with ten carbon atoms. Using the molecular weight of free and combined acid in the volatile oil, no satisfactory results are obtained. The data computed for acids with six, ten and sixteen carbon atoms, respectively, are herewith tabulated.

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[31] See letter to E. K., Jan. 5, 1911.

[32] See letter to E. K., Feb. 6, 1900.

	$C_6H_{12}O_2$	$C_{10}H_{16}O_2$	$C_{16}H_{32}O_2$
For an acid value of 30	6.31 per cent	9.21 per cent	18.71 per cent
For an ester value of 225	57.80 " "	80.35 " "	114.10 " "

FREE FATTY ACIDS OF THE PULP

In endeavoring.to explain the formation of the ethyl esters that constitute the so-called volatile oil, it seemed more rational to assume that the free fatty acids of the pulp, rather than the fatty glycerides of the seed, are primarily instrumental. In connection with the moisture determinations, it has already been pointed out that the computation of the loss of volatile matter as water introduces an error that can be corrected by the xylene method. The odor of the vapors when the berries are dried in the ordinary manner clearly reveals the presence of free fatty acids. Their quantitative determination, however, was desirable in order to ascertain whether a sufficient amount of free acids is present to account for the formation of the volatile oil obtained. For this purpose the berries were extracted with volatile solvents after they had previously been dried in a vacuum over caustic potash.

In the first set of experiments the dried berries were first extracted with heptane, and then with ether. In a second set ether alone was used. In each case the amount of extractive was ascertained by difference, the loss in weight of the substance in the extraction thimble being computed as the amount of extractive in question, the method of weighing thimble and contents described in *Bulletin 107* of the Bureau of Chemistry, U. S. Department of Agriculture, being followed.

	Experiment I.		Experiment II.	
	A.	B.	A.	B.
Heptane extract	39.98 per cent	40.57 per cent	....	....
Ether extract	14.44 " "	10.27 " "	40.77 " "	41.22 " "
Total extract	53.42 " "	50.84 " "	....	....

The acid and ester values of all of the extracts were then determined and the saponification values computed. The results are again tabulated for convenient comparison.

	Experiment I.						Experiment II.	
	Heptane Extr.		Ether Extr.		Total		Ether Extr.	
	A.	B.	A.	B.	A	B.	A.	B
Acid value	22.2	24.4	7.9	4.2	30.1	28.5	31.1	32.2
Ester value	71.4	69.6	0.4*	10.9	....	80.4	75.6	76.8
Sap. value	93.6	94.0	....	15.1	....	108.9	106.7	109.0

It becomes apparent from the above results that the totals of both experiments approximate each other with sufficient closeness. The striking differences, however, between the two sets of experiments is this, that the heptane apparently does not extract the acids and esters from the pulp with the same readiness as does the ether, though the total of extractive of the combined extracts is greater than that of the ether extract alone. Possibly it should be mentioned that the color of both heptane and ether extracts was reddish and that the ether extract was completely soluble in alcohol. The glycerin content of the ether extract was found to be 13.4 and 14.86 per cent respectively in two determinations. For further characteristics of the fatty oil extracted with ether see Fatty Oils.

ESTERIFICATION AT ROOM TEMPERATURE

To determine the rate of esterfication over a long period of time at room temperature, the various acids occurring in saw palmetto berries, namely caproic, caprylic, capric, lauric, palmitic and oleic were each mixed with ethyl alcohol and stored in glass stoppered bottles. A molecular proportion between acid and alcohol of one to twelve was used as it was necessary to economize with some of the acids. These were Kahlbaum's c. p. products, while a nearly absolute alcohol was used from which aldehydes had been removed by caustic potash. The following table gives the quantities of these substances used to make the solutions in the molecular proportion 1:12.

	Mol. Wt. Acid	Mol. Wt. Alcohol	Acid Used	Alcohol
Caproic	116	46	29.0 grams	138 grams
Caprylic	144	46	36.0 "	138 "
Capric	172	46	21.5 "	69 "
Lauric	200.2	46	50.0 "	138 "
Palmitic	228	46	57.0 "	138 "
Oleic	282	46	70.5 "	138 "

After standing two days, the amount of free acid and the amount of ester were determined. (Aug. 16.) The free acid was titrated with alcoholic KOH, using phenolphthalein as indicator. A two gram sample of the acid-alcohol mixture was weighed out, then diluted to about 50.00 c. c. with alcohol to facilitate the titration and later saponification. As the end point with phenolphthalein is not very sharp in the presence of a large amount of alcohol about four drops were used in each titration. After neutralization of the excess of acid, the mixture was heated with an excess of alcoholic KOH for saponification for 1½ to 2 hours, or longer. After cooling, the excess of alkali was titrated back with aqueous sulphuric acid. By calculation, from two determinations which checked fairly well, the amounts of ester were computed in each case. These determinations were repeated at more or less regular intervals and the results tabulated separately for each acid.

During the standing for such long periods of time, some of the alcohol evaporated from the mixture because of poor fitting glass stoppers. This manifested itself in the acid and ester numbers but particularly in the saponification numbers. The saponification number will of necessity remain constant under the best conditions of the experiment, that is, when neither alcohol nor acids evaporate from the mixtures. If only the alcohol content of the mixture was decreased by evaporation, the acid and ester numbers, as found, can be recalculated on the basis of the proper saponification number in the following way. If the alcohol evaporated the remaining liquid would have a higher saponification number. The acid and ester numbers will be proportional to this higher saponification number found. By multiplying the acid and ester values as determined by the ratio of the correct saponification number of the original mixture to the determined saponification number of the altered mixture, we get the actual acid and ester numbers as we would have had, had no alcohol evaporated. By multiplying the average percentages of ester by this same ratio we get the actual percentage of esters. The corrected values are in heavy type in the table and these values are used for the curves. Only those values were corrected where the saponification showed considerable deviations from the true saponification numbers.

Caproic Acid

Date	Acid No.	Ester No.	Sapon. No.	Average percentage of ester
Aug. 16, 1912	86.80	8.40	95.20	2.35
	86.70	9.96	95.66	
Aug. 23, 1912	84.40	5.56	89.96	1.37
	85.11	5.01	90.12	
Aug. 26, 1912	84.53	4.46	88.99	1.14
Oct. 7, 1912	83.00	8.40	91.4	2.23
	82.80	8.95	91.75	
Nov. 11, 1912	81.42	16.10	97.52	4.01
	81.34	15.10	96.44	
	79.60	15.20	94.80	3.91
Feb. 5, 1913	81.80	33.77	115.57	8.53
	84.25	32.62	116.87	
	67.75	27.10	94.85	6.97
Sept. 4, 1913	79.60	47.60	127.20	12.40
	79.50	49.28	128.78	
	58.95	35.90	94.85	9.24
Dec. 23, 1914	86.20	109.90	196.10	28.74
	88.35	113.70	202.05	
	41.66	53.40	95.66	13.72

Caprylic Acid

Date	Acid No.	Ester No.	Sapon. No.	Average percentage of ester
Aug. 16, 1912	81.89	6.85	88.74	1.94
	81.93	5.82	87.75	
Aug. 23, 1912	80.73	5.98	86.71	1.71
	81.38	5.16	86.54	
Aug. 26, 1912	80.22	2.52	82.74	0.77
Oct. 7, 1912	76.77	8.10	84.87	2.50
	76.61	8.24	84.85	
Nov. 11, 1912	76.77	19.37	96.14	4.39
	77.27	14.14	91.41	
Feb. 5, 1913	74.36	31.50	105.86	9.83
	74.87	31.48	106.35	
Sept. 4, 1913	53.34	38.28	91.62	12.40
Dec. 22, 1914	62.50	82.14	144.64	24.28
	60.43	76.00	136.43	
	37.61	48.38	85.99	14.85

Lauric Acid

Date	Acid No.	Ester No.	Sapon. No.	Average percentage of ester
Aug. 16, 1912	76.20 76.20	6.73 7.13	82.75 82.33	2.82
Aug. 23, 1912	74.10 75.00	4.04 3.32	78.14 78.32	1.49
Aug. 26, 1912	74.36	3.52	77.88	1.42
Oct. 7, 1912	70.53 70.82	7.52 5.27	78.06 76.09	3.06
Nov. 11, 1912	68.33	13.00	81.33	5.29
Feb. 5, 1913	63.28 63.90	24.74 25.84	88.02 89.74	10.26
Sept. 4, 1913	42.91 42.94	32.27 28.98	75.18 71.92	12.37
Dec. 22, 1914	40.13 41.48 36.58	45.72 46.51 41.38	85.85 87.96 77.92	16.29 14.62

Palmitic Acid

Date	Acid No.	Ester No.	Sapon No.	Average percentage of ester
Aug. 16, 1912	42.96 43.11	7.14 6.53	50.10 49.64	3.46
Aug. 23, 1912	42.93 42.95	8.39 8.95	51.32 51.90	4.30
Aug. 26, 1912	43.91	3.49	47.40	1.72
Oct. 7, 1912	38.26 39.22	6.00 6.37	44.26 45.50	3.14
Nov. 11, 1912	40.41	10.34	50.75	5.33
Feb. 5, 1913	40.08 40.00 35.46	15.82 17.02 14.54	55.90 57.02 50.00	8.33 7.33
Sept. 4, 1913	40.07 39.97 29.66	27.19 27.72 20.33	67.26 67.69 49.99	13.88 10.25
Dec. 22, 1914	38.54 38.70 29.27	27.38 27.30 20.72	65.92 66.00 49.99	13.86 10.50

Oleic Acid

Date	Acid No.	Ester No.	Sapon. No.	Average percentage of ester
Aug. 16, 1912	67.40	6.51	73.91	3.36
	68.22	5.61	73.83	
Aug. 23, 1912	67.66	8.37	76.03	4.85
	67.83	9.16	76.99	
Aug. 26, 1912	66.48	3.62	70.10	2.00
	....	....	....	
Oct. 7, 1912	62.91	6.84	69.74	3.85
	63.21	7.14	70.35	
Nov. 11, 1912	61.11	12.71	73.82	7.13
	61.62	12.65	74.27	
Feb. 5, 1913	57.23	19.22	76.45	10.68
	57.75	18.90	76.45	
Sept. 4, 1913	38.08	17.60	55.68	10.00
	38.28	18.45	56.73	
	50.37	23.70	74.07	13.26
Dec. 22, 1914	35.28	39.07	74.35	21.45
	34.62	38.48	73.11	

To determine the completeness of esterification at room temperature after 861 days, 20 c.c. of the mixtures of acid and alcohol, as given under the esterification experiments, were shaken up with an excess of sodium carbonate and water. In this way the free acid united with the carbonate to form soluble soaps in most instances, and the alcohol dissolved in the water, leaving the ester formed, which rose to the surface. This experiment was carried out in a cassia flask so that the resulting ester could be measured.

In the case of the caproic acid-alcohol mixture the volume of ester resulting was 5.65 c.c. and 5.40 c.c. from 20.00 c.c. of the mixture. As some of the alcohol had evaporated from the mixture on standing, this gave the large amount of ester from 20.00 c.c. of the remaining mixture.

Twenty cubic centimeters of the caprylic acid-alcohol mixture gave 4.17 c.c. and 4.32 c.c. Here, too, some evaporation had occurred.

The lauric acid-alcohol mixture gave 2.46 c.c. and 2.30 c.c. from twenty cubic centimeters.

The palmitic acid-alcohol mixture and the oleic acid-alcohol mixtures solidified on addition of sodium carbonate and water, so that these had to be warmed to cause solution. Only one sample of the oleic acid-alcohol mixture gave a slight layer of an ester amounting to 0.375 c.c.

Because no layer of ester manifested itself it was thought that this ester might be redissolved in the soap solution. To determine this fact, the soap alcohol-water mixture was shaken out with ether, and the ether evaporated. No residue remained in the case of oleic acid and only a slight amount (0.1322 grams) resulted from 20.00 c.c. of the palmitic acid-alcohol mixture. From analysis this residue was found to be nothing but free palmitic acid, though the analysis shows a very small amount of ester, but the total of acid and ester is considerably over 100 per cent.

No doubt the sodium carbonate and water on heating, as is necessary, decomposes any ester that formed.

The available esters were analyzed and found to be nearly pure. The ethyl caproate analyzed to 94.56 and 92.1 per cent, the caprylate to 93.30 and 94.95 per cent and the laurate to 99.00 per cent. The impurity no doubt was moisture, as the esters were not dried before analysis.

DETECTION OF ALCOHOL IN THE BERRIES

The formation of ethyl esters of the fatty acids contained in the saw palmetto berries by contact with added ethyl alcohol having been demonstrated, both in the berries and *in vitreo* it seemed desirable to ascertain whether the berries themselves supplied any of the alcohol necessary to the formation of the esters. As has been pointed out in the review of previous chemical work on saw palmetto, several investigators report volatile oil though they do not seem to have isolated any; they certainly do not describe it. It is true that traces of so-called volatile oil may be accounted for by the small amount of free fatty acids volatilized either by exposure or distillation with steam. Moreover, it has been observed that the disagreeable odor of the fatty acids characteristic of the fresh berries was displaced more

or less by a rather pleasant odor when the berries had been kept in well stoppered bottles. Assuming that this more pleasant odor was due to ethyl esters, it became evident that the alcohol must have formed in the berries. Hence, it seemed desirable to make a direct test for ethyl alcohol.

For this purpose about 120 grams of pulp and skins were distilled with a solution of potassium hydroxide, which not only fixed the free fatty acids, but which also would set free any ethyl alcohol, if such were present as ester. On account of the formation of soap, this solution foamed to such an extent that the distillation could not be continued even with a layer of paraffin. The experiment was repeated with barium hydroxide which gave better results. 100 c.c. of distillate were collected and this distillate redistilled with potassium hydroxide, only six to eight cubic centimeters being collected the second time. With iodine, this distillate gave the iodoform test, this substance being recognized by its odor and by the crystalline precipitate formed. Brine, in which berries had been preserved, gave similar results. The addition of alkali in the above experiments produced noteworthy color changes due, no doubt, to the pigment of the skins. The alkali also set free basic substances which are volatile and impart their peculiar odor to the distillate.

FATTY OIL

Fatty Oil from Entire Fruit

Unlike the so-called volatile oil, which was observed in the fresh berries preserved in alcohol in amounts too small to be isolated, the fatty oil of saw palmetto forced itself upon the attention of the early investigators because in the percolation of the drug it was apt to separate from the hydro-alcoholic percolate. Hence it receives mention by Read (1892), C. A. S. (1892), Dixon (1894), Sherrard (1894), and Rusby, Bastedo and Coblentz (1895). Sieker, (1897) however, appears to have been the first to have studied the physical constants of the oil, obtained in the manner indicated above. The first and only detailed study of the fatty oil extracted from the seeds was made by Sherman and Briggs in 1899. They found that the oil consisted essentially of the glycerides of caproic, caprylic, lauric, palmitic, and oleic acids and possibly stearic acid.

Without endeavoring to duplicate the admirable work of the investigators last mentioned, it seemed desirable to learn more about the relation of the fatty oil to the several parts of the fruit, also about the relation of the three oils thus obtained to each other. The material which all of the earlier investigators had in hand appears to have been obtained from the entire fruit, either fresh and preserved in alcohol, or dried. The fatty oil of which Sherman and Briggs studied the chemical composition was obtained, in one instance from the seeds, in another by the expression of the entire fruit preserved in alcohol. The problems studied in connection with the formation of the so-called volatile oil, the one for which this investigation was primarily undertaken, however, rendered it desirable to learn something about the fats, glycerides, or free acids, contained in skin and pulp as well as seed. Hence, heptane and ether extracts were prepared from each of these three parts of the fruit.

For this purpose the parts of the berries were dried in a vacuum at room temperature over stick caustic potash. The materials thus dried were comminuted as thoroughly as their nature would permit and extracted in a Soxhlet apparatus for a period of not less than 18 hours in any case. The heptane used was that obtained from Digger's pine, hence of definite boiling point and composition. The amount of extraction was not ascertained by evaporation of the heptane, which boils at 98°C., but by difference in the weight of capsule and contents before and after extraction. Thus extracted, the skins yielded about 9 per cent of heptane extractive, the pulp 39 per cent, and the seeds 10.5 per cent (For detailed figures see the accompanying table.) In the determination of the acid and ester values considerable difficulty was experienced in ascertaining the end point of the reaction more particularly of the ester values. This was due, partly to emulsions that formed on shaking, partly to color reactions produced especially by the pigments of the skins. This difficulty was overcome, in part, by avoiding water as much as possible.

The materials that had apparently been exhausted with heptane, after drying over sulphuric acid in a vacuum and weighing, were then extracted with ether. Considerable additional ether extractive was obtained; the skins yielding about 8 per cent, the pulp about 12 per cent, and the seeds about 5.5 per cent. Of these ether extracts, the acid and ester numbers were likewise determined. The ethereal solution of the extractive from the skins was of a deep green color, that of the pulp reddish, and that of the seeds yellow. The detailed results of the several extractions, also the acid and ester values will be found in the accompanying table.

Heptane-ether extract

		Wt. of dried material used in grams	Extracted with Heptane		Extracted with Ether		Total extracted in per cent	Acid No. heptane extract	Ester No. heptane extract	Acid No. ether extract	Ester No. ether extract	Sap. No. heptane extract	Sap. No. ether extract
			Wt. in grams	Percentage	Wt. in grams	Per centage							
Skins	A	5.5670	0.4584	8.23	0.4546	8.15	16.38	6.02	25.70	1.81	3.97	31.75	5.78
	B	5.2727	0.5244	9.94	0.4304	8.16	18.10	6.33	25.06	1.59	4.77	31.39	6.36
Pulp	A	4.7278	1.8432	38.98	0.6826	14.44	53.42	22.21	71.36	7.876	0.35	93.57	8.226
	B	4.9020	1.9892	40.57	0.5032	10.27	50.84	24.36	69.57	4.17	10.85	93.93	9.53
Seeds	A	9.1868	0.9541	10.38	0.2145*	2.33*	12.71	4.77	23.18	1.68	1.50	27.95	3.18
	B	9.7564	1.0398	10.66	0.5331	5.47	16.13	5.88	20.00	1.92	1.66	25.88	3.58

*These results are evidently due to some unaccountable accident in the experiment.

The difficulties encountered in the determination of acid and ester values being attributed in part to the heptane, extraction with ether alone was restored to. The results obtained are herewith tabulated without further comment.

Ether extract

		Wt. of dried material used	Material extracted	Material extracted	Acid No.	Ester No.	Sapon. No.	Acid No. on oil	Acid No. on oil	Sapon No. on oil
Skins	A	9.5435 grams	0.8627 grams	9.04 per cent	14.57	18.89	33.46	161.3	209.0	370.3
	B	9.9334 "	0.8685 "	8.74 " "	15.16	18.20	33.36	173.4	209.9	383.3
Pulp	A	4.8472 "	1.9766 "	40.99 " "	31.06	75.55	106.62	76.2	183.5	259.7
	B	4.1400 "	1.7058 "	41.22 " "	32.20	76.81	109.01	76.3	186.6	262.9
Seeds	A	10.1314 "	1.0650 "	10.51 " "	7.30	22.88	30.18	69.4	217.6	287.0
	B	9.6368 "	1.0028 "	10.41 " "	7.40	22.92	30.32	71.2	220.3	291.5

Previous to the extraction experiments, the results of which are tabulated in the preceding table, dried skins, pulp, and seeds had been extracted with heptane. The difficulties encountered in the determination of the acid and ester values, referred to above, had not been overcome sufficiently to render the results obtained worth while recording. The results obtained in the heptane extraction, however, may be worth recording for the sake of comparison.

Heptane extract

	Amount of material used	Amount of extract	Percentage of extract
Skins—A	5.2980 grams	0.9314 grams	17.64
B	5.7011 "	1.0220 "	17.92
Pulp A	3.4817 grams	1.4943 grams	42.92
B	3.1692 "	1.3297 "	41.90
Seeds A	7.0067 grams	1.0920 grams	15.58
B	6.8413 "	1.0506 "	15.35

FATTY OIL FROM SEEDS

In order to obtain a somewhat larger amount of fatty oil from seeds, the latter were reduced to as fine a condition as possible and extracted with ether in a percolator. After the extraction had progressed for a length of time, the seed meal was dried by exposing to air and the meal ground to a fine powder, when this powder was further extracted with ether but very little extractive was obtained. The two ether solutions were united, the ether evaporated spontaneously and the oil dried over sulphuric acid. The resulting oil had a brownish color and contained solid matter in suspension, probably solid fats. The odor was that of oil freshly produced from cotton seeds. Other properties are as follows:

Specific gravity at 27° C	0.9249
Index of refraction (Abbé-Zeiss App.)	1.4596
Melting point	8.0° C
Iodine value (Hanus)	43.47 and 43.67
Acid number	19.94 and 19.67
Ester number	218.2 and 222.6
Unsaponifiable	a. 0.854 per cent b. 1.075 " " c. 1.090 " "
Glycerin	14.860 " "

FATTY OIL FROM SKINS

After drying over caustic potash in a vacuum, the skins were ground as fine as possible, then extracted with ether and the ether allowed to evaporate spontaneously. A solid resulted which was very dark in color varying between brown and dark green. The oil or fat seems to form a kind of suspension when mixed with alcohol. Other properties are as follows:

Melting point (roughly)	40.0° C
Acid number	69.4 and 71.20
Ester number	217.6 and 220.3
Saponification number	287.0 and 291.5
Unsaponifiable	a. 1.008 per cent b. 1.114 " " c. 1.115 " "
Glycerin	4.37 per cent and 6.10 per cent

RELATION BETWEEN FATTY OILS AND VOLATILE OIL

From the experiments on esterification at room temperature, we find that esters form when acids are brought in contact with alcohol for a period of time. It was thought desirable to try the effect of alcohol on the fatty oils of the various parts of the berries, as these oils contain free acids. It is of further interest to see how dry hydrogen chloride gas will affect the esterification. Ordinarily it should be an aid.

Four grams of each of the fatty oils from the seeds, pulp, and skin were mixed in the one case with 25 c.c. of absolute alcohol and in the other with 25 c.c. of alcohol, which contained 3.42 grams dry hydrogen chloride gas which makes an acid of specific gravity of 0.9764 having 14.61 per cent of hydrochloric acid by weight.

The seed oil which is heavier than the alcohol seems to be only partly soluble in the alcohol. This oil is lighter than the alcoholic hydrogen chloride mixture, and only slightly soluble, forming a dark green to brown color.

The oil from the pulp is completely soluble in alcohol giving a yellowish color to the solution. With alcoholic hydrochloric acid it seems to dissolve forming a greenish solution at first, which turns very dark green to brown so deep that the solution is no longer transparent.

The oil from the skins which is really a fat at ordinary temperature forms a kind of grayish suspension in the alcohol while on addition of the alcohol-hydrochloric acid mixture, the fat turns a decided green giving a suspension similar to that with the alcohol, only the suspended matter seems to be more granular.

UNSAPONIFIABLE MATTER

In order to ascertain the amounts of unsaponifiable material extracted with ether from the skins, pulp, and seeds, the following experiments were made. From about one to approximately four grams of so-called oil, *i. e.* ether extractive after evaporation of the solvent, were saponified with an excess of alcoholic potash. After saponification the alcohol was removed by evaporation of the solution to dryness, the addition of water and continued evaporation. The flask was then washed out with about 100 to 150 c.c. of distilled water and finally with 40. c.c. of ether. The soap solution was extracted four to five times with ether, the joined ethereal solutions in turn were washed with water to which a few drops of concentrated solution of potassa had been added, and finally with distilled water. After evaporation of the ether and drying of the residue over sulphuric acid in vacuum the residue was weighed. The results are recorded in the following table:

		Wt. of oil used	Unsaponifiable Material	
			Weight	Percentage
Skins	A	0.8685 grams	0.0272 grams	3.13
	B	4.0390 "	0.1535 "	3.92
Pulp	A	1.7058 "	0.0172 "	1.008
	B	3.9922 "	0.0445 "	1.114
	C	3.0000 "	0.0446 "	1.115
Seeds	A	1.0650 "	0.0091 "	0.854
	B	3.9980 "	0.0430 "	1.075
	C	3.9994 "	0.0436 "	1.090

The unsaponifiable matter in all cases was highly colored; that from the seed yellow, that from the pulp and skins was colored brilliant red. After several days standing over sulphuric acid in a vacuum the color of the residue from the skins faded to yellow and finally to white. The unsaponifiable matter of the pulp, however, maintained its yellow color. A very strong odor of withered rose petals permeated the whole room in the case of the unsaponifiable matter from the seeds. A similar odor came from the unsaponifiable matter of both pulp and skin but this turned to the odor of carrots when in the yellow stage.

The above mentioned color no doubt was the material that prevented sharp end points in the saponification experiments.

Tests for phytosterol were made on all the unsaponifiable material but all of the tests showed negative results, therefore no phytosterol was present.

ENZYMES

Even though it had been demonstrated that the esters of the fatty acids found in the berries can and do form the ethyl esters by mere contact with ethyl alcohol, it still remained of interest to learn whether an enzyme existed in the berries that might be expected to facilitate or hasten the reaction when the fruits are preserved in alcohol. In this connection it should be mentioned that the original odor of the fresh berries, due to the free fatty acids present therein, gives way in part to the more pleasant odor of the ethyl esters in less than an hour when the fruits are covered with 95 per cent alcohol.

The hydrolytic enzyme, which might be supposed to accelerate the condensation of ethyl alcohol and the fatty acids and which would be of special interest in this connection, is the lipase. Fresh berries having been turned over to Professor H. Bradley, were found by him to contain a considerable amount, relatively speaking, of vegetable lipase.

Inasmuch as 80 per cent alcohol is one of the substances which according to Pierce,[33] inhibits the enzyme activity of lipase more effectively even than sodium fluoride, it became necessary to learn whether the alcohol, in the amount in which, it was added to the berries, was diluted sufficiently by the water content of the fruit to bring its ethyl hydroxide content below the 80 per cent limit. For this reason the ethyl hydroxide content of the liquid in which fresh berries had been pickled for ten months was ascertained. At the same time the acid and ester values were also determined, five grams of liquid being used for each determination.

	$\frac{N}{2}$KOH	Acid No.	Ester No.
1) Alkali used for neutralization of free acids	0.93 c. c.	5.21	
1a) Alkali used for neutralization of free acids	0.94 " "	5.26	
2) Alkali used for saponification of esters	1.97 " "		11.03
2a) Alkali used for saponification of esters	1.56 " "		8.75

For the determination of the alcohol the standard method[34] was employed, 100 c.c. of the liquid being weighed at 15°.6. After the specific gravity of the distillate had been taken, it was saponified, the saponification liquid again distilled and the specific gravity taken a second time for the purpose of ascertaining to what extent the free fatty acids and esters had influenced the first determination. The alcohol content is recorded in percentage by weight.

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[33] *Journ. of Bio. Chem.*, 16, p. 13, (1913).

[34] *Bulletin 107* (revised) of the Bur. of Chem., U. S. Dept. of Agr., p. 95.

Wt. of 100 c.c. of liquid used	Sp. gr. of first distillate	Percentage of alcohol	Sp. gr. of second distillate	Percentage of alcohol
94.2112 grams	0.9216	51.38	0.9247	47.00
94.5674 "	0.9216	51.19	....	....

The specific gravity of the so-called volatile oil as specially prepared by Lloyd, having been found to be 0.8627, it will be seen that its presence naturally has a tendency to slightly lower the density of a spirit of less than 50 per cent, hence to increase to the same slight extent its apparent alcohol content. The difference, however, is slight as compared with that between 47 per cent, the actual amount of ethyl hydroxide in the pickling liquid, and 80.0 per cent the strength at which ethyl hydroxide inhibits the enzyme action. The question, nevertheless, may yet arise whether the ethyl hydroxide does not get in some of its injurious work before it is sufficiently diluted by the water contained in the pulp.

In order to ascertain the presence of oxidizing enzymes, solutions that might be expected to contain oxydase were prepared from the skin, pulp, and seeds of berries that had been preserved in ether, chloroform-water, alcohol, and brine respectively. When tested with tincture of guaiac which gave an excellent test with an extract of the shoots of cucumber, no positive reactions were obtained.

Like solutions were tested with freshly crystallized hydrothymoquinone,[35] but also with negative results.

In the preparation of the above aqueous solutions the oily constituents of the fruit or rather the parts thereof used, were removed by ether or petroleum ether.

Both solution and pulpy residue were likewise tested with hydrogen peroxide. The solution did not react with this reagent. After having stood for four months in the preserving liquid, the pulp of the berries preserved under brine gave only small bubbles with hydrogen peroxide. That from the berries preserved in chloroform water gave no signs of gas, but the small bubbles produced by the material preserved in alcohol came off readily.

After standing for a day or two, the several materials showed increased activity of gas formation in contact with hydrogen peroxide solution. The pulp and seeds of the berries preserved in brine formed large bubbles. The pulp alone of the same material comes next; then follow the pulp of the berries preserved in alcohol, chloroform-water, and ether, in the order mentioned.

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[35] Nellie Wakeman, *Phytochemistry for Pharmacy Students*, p. 7.

CARBOHYDRATES

Read (1879), who appears to have been the first to have subjected saw palmetto to a preliminary chemical survey, reports the presence of "saccharine matter" in the berries, likewise does C. A. S. (1892). Sherrard (1894) also reports the presence of "sugar" and starch. Coblentz (1895) reports the presence of glucose and dextrin in the pulp and of sugar in the seeds. Sherman and Briggs (1899) stated that "large amounts of sugars were found in the fruit, apparently in the pulp, whereas "cutose" appears to be contained in the skins. A small amount of pentose was also found. As much as 5.4 per cent of sugars was estimated as being present, the bulk of which was in the form of invert sugar, "and but little as cane sugar."

The invert sugar found by Sherman and Briggs will readily account for the formation of alcohol in the berries already reported. Nevertheless a further insight into the carbohydrate content of the fruit, more particularly of its several parts, skin, pulp, and seeds seemed called for. For this reason the following experiments may be worth recording, though they do not carry us beyond a preliminary survey in this direction.

The skin, pulp, and seeds, that had previously been extracted with ether (see under fatty oil) were successively extracted with cold water, hot water, cold alcohol, hot alcohol, and finally with ethyl acetate. The resulting solutions were immediately evaporated in vacuum to a small volume in order to avoid decomposition of the aqueous extracts.

Following the outline of Haas and Hill,[36] these solutions were first tested for pentoses.

After subsidence of suspended matter, the supernatant liquid was used in each test. In some instances where the suspended material would not settle, or in case the solution was colored, it was first treated with alumina cream and then filtered. The reagents used for the tests were aniline acetate, orcinol, orcinol and ferric chloride, and phloroglucinol. These tests were carried out as follows: On distillation of the material with hydrochloric acid pentosans are hydrolized to pentoses and these in turn are converted to furfurol. Furfurol turns aniline acetate (made by mixing equal parts of aniline and acetic acid) red. The distillate is allowed to impinge on filter paper saturated with the aniline acetate.

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[36] *The Chemistry of Plant Products*, p. 55.

A pentose warmed with hydrochloric acid and orcinol produces a greenish yellow color which is soluble in amyl alcohol to a clear green solution. In Bial's modification of the orcinol test, one gram of orcinol is dissolved in 500 c. c. of water; 30 c. c. of concentrated hydrochloric acid and 20 drops of official ferric chloride solution are added. When a pentose is heated with 4 to 5 c. c. of this reagent, a green coloration results and later precipitation. This test is characteristic for pentoses.

When phloroglucinol is substituted for orcinol, a red color results with production of a brown precipitate soluble in amyl alcohol.

Pentoses also form osazones and reduce Fehling's solution.

Pentoses in Skin Extract

	Aniline acetate	Orcinol	Bial's Orcinol test	Phloroglucinol
Cold water extract				
Hot water extract			Good test, color and precipitate	Good test, color and precipitate
Cold alcohol extract				
Hot alcohol extract				

Pentoses in Pulp Extract

Cold water extract	Color	Color	Color and precipitate.	Color and precipitate.
Hot water extract			Color and precipitate, slow in coming.	No test.
Cold alcohol extract				No test.
Hot alcohol extract			Faint test, no precipitate.	No test.

Pentoses in Seed Extract

Cold water extract	Very faint color.	No color.	No color.	Excellent test.
Hot water extract	Faint color.	Poor color.	Very light green.	No test.
Cold alcohol extract	No test.	No test.	No test.	No test.
Hot alcohol extract	No test.	No test.	No test.	No test.

To ascertain the presence of sugars the rotatory power of each solution was determined, using a 5 cm. tube, and the experiment performed at room temperature. The cold water extract from the pulp of unknown concentration showed a dextro-rotation of 3.33°, and the combined hot and cold water extract of the skins gave a dextro-rotation of 1.93°. This would indicate the presence of a dextro-rotatory substance.

In order to find out if a disaccharide or glucoside is present each solution was hydrolized by boiling with a small amount of concentrated hydrochloric acid. In no case was there a change of rotation, indicating the absence of either disaccharide or glucoside.

With phenyl hydrazine, in acetic acid solution, a yellow brown precipitate formed with the syrupy solution of the skins. The unpurified material gave a melting point of 199°C. When thoroughly washed with water, the melting point became 187-189°C. This osazone is soluble in hot 60 per cent alcohol and in a large quantity of water, but does not come down in crystals, but in a more or less gelatinous form. On heating the impure sample for an extended period of time at 105°C., it also had a melting point of 189°C.

This material was not soluble in 94 per cent alcohol but colored the alcohol slightly. This colored solution showed no rotation in the polariscope. The tests made are in part those which would answer for galactose.

At a later time some of this syrupy material from the skins in water solution was treated with basic lead acetate for purification and the excess acetate disposed of with anhydrous sodium sulphate. A beautiful yellow precipitate resulted. This when dried had a melting point from 189°-190°C.

GLUCOSIDE

As previously stated under carbohydrates, all of the extracts obtained from skins, pulp, and seeds with cold and hot water, with cold and hot alcohol, also with ethyl acetate were hydrolized after the optical rotation had been determined. Inasmuch as no change in the angle of rotation was observed, the conclusion seems warranted that neither disaccharide nor glucoside is present in these solutions. This is contrary to the statements made by C. A. S. (1892) and C. C. Sherrard (1894), but it is in agreement with the statement made by Sherman and Briggs (1899).

ALKALOID

Coblentz (1895) states that saw palmetto berries contain "traces of an alkaloid" but does not mention how he detected its presence. Sherman and Briggs (1899), however, claim that alkaloids are entirely absent.

While distilling the berries with potassium hydroxide, also with barium hydroxide, for the purpose of determining the alcohol content of the berries, it was observed that the distillate had the odor of some basic substance. Upon the addition of iodine, a blue color resulted, which soon disappeared. It, however, reappeared upon the addition of more iodine and finally the color remained. Soon thereafter iodoform separated. The original blue color may possibly be attributed to a periodide of an organic base, which, however, gave up its iodine so long as any alcohol remained to be converted into iodoform.

A part of the alcoholic distillate with the basic odor was collected in dilute hydrochloric acid. This was devoid of the basic odor and for the purpose of the iodoform test it was redistilled to recover the alcohol. Upon the addition of platinum chloride to the residue, yellow octagonal crystals resulted, apparently the double salt of the base.

In order to ascertain whether the berries contain basic substances as such, a systematic search for alkaloids was made and repeated with several slight modifications. No decided tests, however, could be obtained with the general alkaloidal reagents used.

Hence it may be assumed that the basic substance or substances obtained by heating the berries with an aqueous solution of barium hydroxide, were products of hydrolysis, probably of proteins. The slight indications for alkaloid obtained with some of the general alkaloidal reagents in the special search for alkaloids may likewise be attributed to similar changes on a much smaller scale.

CONCLUSIONS

1. The volatile oil so-called, *i. e.* the mixture of ethyl esters of fatty acids, that is contained in alcoholic galenicals of the drug, is not a volatile oil in the generally accepted sense of the term. Neither is it a so-called ferment oil, resulting upon the hydrolysis of a glucoside, such as the oils of wintergreen, sweet birch, mustard, etc. It is formed by condensation of the free fatty acids, which are naturally contained in the berries, with ethyl alcohol, the preservative. Small amounts of ethyl esters are formed upon fermentation of a sugar, contained in the berries, to ethyl alcohol, if the fresh berries are allowed to stand when they undergo the necessary chemical changes. Considerably larger amounts, however, are formed when, as previously stated, the berries are preserved in alcohol.

2. Mere traces of volatile oil may be obtained from fresh berries, but this does not consist of ethyl esters, at least not to any appreciable extent, but of such of the free fatty acids of the berry as are volatile with water vapor. Owing to the presence of higher fatty acids such an oil is semi-solid. To this extent the true volatile oil of saw palmetto resembles that of the cocoanut, the only other oil of the palm family known at present. Whether a further analogy exists between these two volatile oils cannot be decided until much larger quantities of fresh berries can be distilled, so that sufficient volatile oil for a chemical investigation may be obtained.

3. Although the enzyme lipase has been demonstrated to exist in the berry, its presence is not necessary to explain

the condensation of the ethyl alcohol with the free fatty acids to the corresponding ethyl esters. Indeed the alcohol may even interfere with, if not completely inhibit, the enzyme action if sufficient alcohol could be used. Prolonged contact between the ethyl alcohol and the individual acids has shown that in each case the formation of esters can be accounted for without enzymes or other so-called catalytic agent.

4. The numerous other results obtained in this investigation were either incidental to the main object sought, or were prompted in no small part because the material happened to be available. For all of these details the text proper will have to be consulted.

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Botanical history, description (including constituents, volatile oil, fatty oil, and saccharine matter) and medicinal uses are given.

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Americanische Drogen, 12; *Fructus Sabal serrulata.*
Pharm. Centralhalle, 24, p. 168. (*Amer. Jour. Pharm.*, 55, p. 466; *Yahrb. d. Pharm.*, 18, p. 88; *Yearbook of Pharm.*, 21, p. 225; *Proc. A. Ph. A.*, 32, p. 126.)

An illustrated botanical description of the berries is given. Seed protein is described. *Oxalat druesen.* The solubility of the various parts of the kernel in alkalies and water is recorded. Also the color reaction toward iron salts. The uses to which the berries are put are mentioned.

S——, C. A. 1892.
Saw Palmetto, Sabiana serrulata.
The New Idea, 14, p. 350. (*The Western Druggist*, 14, 12, p. 355.)

Under the title "Original Communication," the author reviews the habitat of this palm, its uses, and the description of the fruit. He mentions two oils, a volatile oil and a fixed oil. Also "saccharine matter." The uses of the juices from the berries are given. The drug is said to contain a very bitter glucoside.

Dixon, J. M. 1894.
The Saw Palmetto.
Proc. Florida Pharm. Assoc. 8, p. ..... (*Proc. A. Ph. A.*, 43, p. 639.)

The author describes the preparation of a fluid extract. The oil which separates is used as an elixir in different forms.

Sherrard, C. C. 1894.
Saw Palmetto (Sabal serrulata).
Proc. A. Ph. A., 42, p. 309.

The article supplies a general botanical description of the palm and of the fruit in particular. The aroma of the latter he attributes to a "volatile oil." The results of a "proximate analysis" are given: moisture, ash, organic constituents (extractive, volatile oil, fixed oil, resin, acids, sugar, gum, albuminoids, glucosides, and starch).

Sieker, F. A. 1895.
Fluid Extract of Sabal serrulata.
Pharm. Rundschau, 13, p. 236.

The results of the examination of two commercial samples of fluid extract (one prepared from "green fruit," the other presumably from dry fruit) are reported; specific gravity, solubility in alcohol and water, alcohol content, extractive.

Schnitzer, ——. 1895.
Serenoa serrulata, Benth. & Hook.
Chemiker Zeitung, 19, p. 167. (*Yahrb. d. Pharm.*, 30, p. 123.)

Rusby, Bastedo, Coblentz. 1895.
The Pharmacology of Saw Palmetto.
Proc. New Jersey Pharm. Assoc., 25, p. 45. (*Yahrb. d. Pharm.*, 31, p. 161; *Proc. A. Ph. A.*, 44, p. 534.)

The author on the "Botany and Materia Medica" of Saw Palmetto takes up the "botanical position," "habit and appearance," "economic uses mentioning the large amount of tannin, and the large amount of potash in the trunk." The "medicinal uses" and description of the fruit are also recorded.

A very complete histological description is given. A dark brown resin occurs in some of the cells of the pulp. Two oils, one a very light yellow and the other darker, are found in various layers. Calcium oxalate crystals were also found.

Between the endocarp and seed occurs a sticky viscous substance of a sweet oil taste consisting of glucose and oil which is no loger present in the dried fruits. The cells of the tegmen are filled with proteid matter and also contain some fat and oil.

Coblentz studied the benzene, the alcoholic, and the aqueous extracts of the pulp and found the following substances: a volatile oil, traces of an alkaloid, an "indifferent resin," a non-saponifiable oil and a fat; glucose, and a "vegetable acid"; solid extractive containing albumin, dextrin, and glucose.

The seeds contain a fixed extract, sugar, and resin.

The dried berries lose a considerable amount of "fixed oil," and "fatty matter when further dried for pulverization."

Sargent, C. S. 1896.
The Tree Palms of the U. S.
Garden and Forest, 9, p. 151. (*Yahrb. d. Pharm.*, 31, p. 161; *Am. Jour. Pharm.*, 68, p. 397.)

The author gives an extensive account of the palmetto as to its habitat, its uses as a vegetable, in brush making and in roof making. Nothing chemical is recorded. Some historical data are also recorded, for example that the tree is known as cabbage palmetto.

Trimble, H. 1896.
The Tannins of the Palmetto.
Garden and Forest, 9, 182. (*Am. Jour. of Pharm.*, 68, p. 397; *Yahrb. d. Pharm.*, 31, p. 161.)

The author reports the moisture, ash, and tannin content of the dry material (stem and root). Chemical properties and ultimate analysis reveal the close realtionship of the tannin from *Serenoa serrulata* or scrub palm with that from oak bark.

Sieker, F. A. 1897.
Notes on Several Fatty Oils.
Pharm. Rev., 15, p. 113.

Two samples of saw palmetto were extracted with alcohol and the fixed oil examined. The solubility, congealing point, Huebl iodin number, acid, ester, and saponification numbers, also chemical and physical properties are recorded.

Sherman, P. L. and Briggs, C. H. 1899.
Saw Palmetto.
Pharm. Arch. 2. p. 101. (*Proc. A. Ph. A.*, 47, p. 507.)

These authors give the habitat and description of the saw palmetto as well as extraction of the oil. Under the title

"*Distillation of the Oil,*" the properties of fractions are given in tabulated form. The "Composition of the Oil" shows presence of caproic, caprylic, capric, lauric, palmitic, and oleic acids, and esters.

"*Identification of Acids*". The acids were identified largely by melting point, boiling point, and titration. These properties are tabulated. "*Identification of Esters,*" Esters of the above acids with ethyl alcohol were found, but no glycerides. The various esters were fractionated and the acid numbers determined. Tabulated results are given. The composition of the "*Residue from Distillation of Oil*" was undetermined. A tabulated result of the quantitative distillation of the oil is given.

"*Oil of Nuts.*" The nuts contain about 12 per cent of oil soluble in boiling benzene. The chemical and physical properties of this oil are recorded.

"*Distillation of Oil*". This oil differs greatly from the oil of the pulp.

"*Saponification of the Oil of the Nuts*" showed the presence of glycerin in the form of glycerides.

"*Identification of the Fatty Acids in this Oil of the Nuts*". Caprylic, capric, lauric, palmitic, stearic, and oleic acids were identified by melting point, boiling point, and acid number. The results are in tabulated form.

Alkaloids were entirely absent.

"*Determination of Sugars*". Large amounts of sugars were found in the fruit of saw palmetto.

In a portion extracted with alcohol and redissolved in water no tannin was found. "Cutose" was found in the alcoholic extract. No glucoside seemed to be present. "Estimation of Sugars". The inversion method was used. A small amount of pentoses was also found.

Schreiner, O. 1900.
Saw Palmetto Oil.
Pharm. Rev., 18, p. 217. (*Proc. A. Ph. A.*, 48, p. 759.)

The author reviews the earlier contributions on saw palmetto with special reference to the presence of a volatile oil. He concludes that a volatile oil is not present in the dried berries and points out that its presence or absence in the fresh fruit cannot be established by reference to the literature on the subject, but by experiment only.

The Utilization of Saw Palmetto. 1901.
Consular Report, 1900, on Trade of Charleston and District, p. 22. House of Commons 1901, vol 85., *Diplomatic and Consular Reports.* (*Pharm. Journ.*, 66, p. 569.)

The report suggests the palmetto as a source of paper. The tannic acid in the root is as good for tanning as hemlock bark.

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THE CHEMISTRY OF THE OIL OF ACHILLEA MILLEFOLIUM L.

A STUDY IN ECONOMIC DRUG CULTURE

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THE CHEMISTRY OF THE VOLATILE OIL OF ACHILLEA MILLEFOLIUM L.

INTRODUCTION

The genus *Achillea* comprises about seventy-five species which are natives of the Northern hemisphere, mainly of the old world. Of this number possibly eight species grow in North America.

Most of the members of this rather large genus have been considered merely as noxious weeds, but some six or eight have been used more or less as medicinal agents and possibly an equal number have been used by gardeners and horticulturists as ornamental plants.

ACHILLEA MILLEFOLIUM—One species in particular of this genus is of considerable historical interest, namely, *Achillea Millefolium* which is one of our oldest medicinal plants. According to Pliny this genus was named in honor of Achilles, the hero of ancient Greece, who is said to have been the first to use this herb as a vulnerary.

In his work on *Materia Medica*, written A. D. 77–78, Dioscorides mentions three kinds of *Achillea* distinguished by the color of their flowers, white, dark-red, and yellow. These are probably to be referred to *Achillea magna*, *A*, *tanacetifolia* and *A*, *tomentosa*.

The common milfoil was extensively used by Stahl and Haller in the seventeenth and eighteenth centuries, but following this period it fell into comparative disuse among physicians. Outside of the pharmacopoeias little mention of it is found in the medical and pharmaceutical literature of the eighteenth and nineteenth centuries. It is, however, still used as a popular remedy in many countries and is highly valued by some physicians of the Eclectic School of Medicine.

The notion is liable to prevail that because a certain remedy has been omitted from the pharmacopoeias it is necessarily not only worthless but harmless. On the contrary many plants which were formerly official are capable of producing powerful effects and should be used with caution. This is true of the common milfoil which, according to Ronzier-Joly[1] has decided power in promoting the uterine functions.

Though mainly of historical interest, reference may be made to an article published by E. Palmer[2] in 1878 in which he reports upon the medicinal plants used by the North American Indians. He states that the Pah-Utes use the yarrow of the settlers of Utah for weak and disordered stomachs and that it was much used by the whites in the form of bitters.

In a paper presented at the Italian Congress of Physicians in Rome in 1895, Mennella made an effort to rescue milfoil from the disuse into which it had fallen among physicians. He considered the plant to be a valuable remedy in chronic catarrh of the stomach, and believed that it would also, probably, prove to be a valuable cardiac remedy; moreover, that it possessed decided value as a preventive of the formation of stones in the bladder and for their expulsion.

Achillea Millefolium found recognition for a considerable period in nearly all the leading pharmacopoeias of the world. In the Pharmacopoeia of the United States for 1860 and also in the revision for 1870 it was included in the secondary list of the Materia Medica. As late as 1880 it was still recognized by the French Codex, in 1885 by the Belgian Pharmacopoeia, in 1889 by the Austrian and in 1904 by the Mexican Pharmacopoeia. In the last named, however, it is described as being little used.

The best known and most widely used species of this genus is *Achillea Millefolium.* It is native to northern and middle Europe and Asia but has been naturalized in New Zealand, Australia, and North America. In many localities in the central part of the United States it grows abundantly[3] in fields, pastures, and waste places. In this country it is commonly known as yarrow or milfoil. In Germany it has no less than eight popular names, *Schafgarbe* being the most common.

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[1] Bull. *Gén. de Therapeutique.* 1857.

[2] *Am. Journ. Pharm.*, 50, p. 590 (1878).

Despite the fact that milfoil has been widely used through a long period of time, comparatively little is known concerning its chemical constituents. So far the volatile oil has received more attention at the hands of the phytochemist than any other constituent or group of constituents. This is no doubt largely due to its beautiful deep blue color which gives it a rather unique position in this group of plant products. Although several reports have been made on the volatile oil, only two constituents have so far been identified, namely cineol and acetic acid.

The first chemical investigation of milfoil was made by L. F. Bley[4] in 1828, which included a proximate analysis of the root, and also of the herb. The amount of oil obtained from both was so small that nothing was learned concerning them except that both oils were lighter than water, that the root oil was almost colorless, had an unpleasant taste and a faint valerian-like odor and that the oil from the herb had a beautiful blue color somewhat darker than that of chamomile oil.

The next chemical investigation of milfoil was made by Zanon[5] who separated from the herb a bitter principle which he named achillein. This was later shown by von Planta to be a gluco-alkaloid identical with that which he himself had separated from *Achillea moschata.* Zanon also separated an acid which he named achilleic acid, but this was shown by Hlasiwez, in 1857, to be identical with aconitic acid.

In 1862 Ch. C. Sears[6] made a proximate analysis of milfoil herb and reported finding the usual plant constituents.

In 1894 Schimmel & Co.,[7] obtained from milfoil by steam distillation a deep blue oil having a remarkably strong aromatic odor. They were able to identify cineol, though the amount present was so small that it could not be detected by its odor. No data were given concerning physical constants. The blue constituent formed a considerable part of the oil.

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[3] Quite prevalent in California where it was used successfully by local practitioners as an emmenagogue. Report on the Drug market, *Proc. A. Ph. A.*, 27, p. 613 (1879). Very abundant in Kansas. R. J. Brown. *Ibid.*, 29, p. 441 (1881).

[4] Trommsdorff's *Neues Journal der Pharmacie*, 16, I, pp. 245–273 (1828). *Ibid.*, 16, II, pp. 94–120 (1828).

[5] *Ann. d. Chem. u. Pharm.*, 58, pp. 21–29 (1846.)

[6] *Journ. Md. Col. Pharm.*, 2, p. 74; *Proc. A. Ph. A.*, 10, p. 113 (1862).

[7] *Report of Sch. & Co.*, Oct. 1894, p. 55.

In 1902 A. Aubert[8] analyzed a sample of milfoil oil which had been distilled by Metzner and Otto, Leipzig. The following data were given: slight acid reaction, $d_{22°}$ 0.9217, $n_{D20°}$ 1.506. The oil was fractionated under diminished pressure, all fractions having a more or less blue color. A test was applied for cineol but the result was not satisfactory. With sodium bisulphite the oil formed a slight precipitate which, on being decomposed by potassium hydroxide, gave a substance having the odor of cedar wood. This was taken to indicate the presence of an aldehyde. From elementary analyses and molecular weight determination the blue constituent was regarded as a hydrocarbon of the composition $C_{12}H_{20}$. Aubert considered the blue constituent to be different from that of chamomile oil.

The latest report upon milfoil oil is that of Arthur Sievers[9] published in 1907. By steam distillation he obtained three samples of oil.

1. The first was from comparatively fresh material (whole plant). The yield was 0.235 per cent based on the weight of undried material. The color of the oil was deep blue which had not changed appreciably after standing almost two years. Sp. gr. of the fresh oil was 0.8687; after nearly a year and a half it was 0.8760 at 18°. The saponification number was 37.7 corresponding to 13.2 per cent of ester calculated as bornyl acetate. The saponification number after acetylation was 74 (average) corresponding to 20.35 per cent total alcohol and 10.08 per cent of free alcohol calculated as $C_{10}H_{17}OH$.

2. The second sample of oil was obtained from the dried herb. The yield was 0.237 per cent based on the weight of the dry material. Color was similar to first sample. Sp. gr. was 0.8873; nearly a year and a half later it was 0.8935 at 18°.

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[8] *Journ. Am. Chem. Soc.*, 24, p. 778 (1902).

[9] *Pharmaceutical Review*, 25, pp. 215–218 (1907).

The saponification number was 29.3 corresponding to 10 per cent of ester calculated as bornyl acetate. After acetylating the saponification number was 66.4, corresponding to 19.25 per cent total alcohol and 11.25 per cent of free alcohol calculated as $C_{10}H_{17}OH$.

3. The third sample of oil was obtained from the fresh flowers. The color of this oil was also deep blue.

A portion of the oil from the entire plant was saponified, the color remaining unchanged. The sp. gr. of the saponified oil was 0.864 at 18°. The oil was fractionated but no compound was identified. In the saponification liquid acetic acid was identified.

Achillea Ageratum—This plant grows abundantly in central Italy where it is frequently cultivated in gardens on account of its very handsome yellow flowers. It has also been used to some extent medicinally. The odor of the plant is strongly camphoraceous when rubbed between the hands. The only chemical investigation of this plant is that made by De Luca[10] in 1875. The yield of oil from plants collected during the flowering period was very small, from plants collected just before the flowering period it was larger. No definite statement of the yield is given. The density of the oil at 24° was 0.849. The fraction of the oil boiling at 180-182° was subjected to elementary analysis, the results agreeing with the formula $C_{26}H_{44}O_8$. The oil was treated with chlorine and also with bromine but no halogen derivative was isolated. This seems to be the only investigation made of this oil, consequently none of its constituents are known.

Achillea Moschata—This plant grows in Switzerland at an altitude of 1500 to 3400 meters and like all Alpine plants it is very small. It has been used in Switzerland for centuries as a stomachic, nervine tonic and a febrifuge. It is used in the preparation of liquors in the same manner that *Artemisia absinthium* is used in France. In its external characters it resembles ordinary milfoil. Its odor resembles that of musk.

In 1870 A. von Planta-Reichenau[11] made a somewhat extended chemical investigation of this plant using the above-ground portion, collected before flowering. He obtained the following: 1. A bluish-green volatile oil of a peculiar, though not disagreeable odor and a taste somewhat similar to that of peppermint. The sp. gr. was 0.9346 at 15°. The oil began to boil at 170°, the greater part of it distilling between 180° and 210°. The distillate between 230° and 260° was brown and had the odor of wormwood. Elementary analyses were made of fractions 170°-190°, 190°-210°, and 210°-230°, the results agreeing with the formula $C_{12}H_{20}O$. Von Planta considered the oil to be composed of a single volatile substance and a resinous substance.

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[10] *Ann. Chim. Phys.*, 4, pp. 132–134 (1875).

[11] *Annalen*, 155, pp. 145–160 (1870).

Without stating any reason for it, he gives for the pure oil boiling at 170°-210° the formula $C_{24}H_{40}O_2$ as probable. This portion of the oil he named ivaol.

2. Ivain, $C_{24}H_{42}O_3$, a yellow bitter principle, insoluble in water, soluble in alcohol.

3. Achillein, $C_{20}H_{38}N_2O_{15}$, a brownish-red, amorphous, very hygroscopic substance having a very bitter taste and an alkaline reaction, readily soluble in water, with more difficulty soluble in absolute alcohol, insoluble in ether.

4. Moschatin, an odorous principle of an aromatic bitter taste, somewhat soluble in alcohol, almost insoluble in water.

5. Stearic acid.

In 1880 Bernard [12] published an article on *Achillea moschata* in which he reviews the work of von Planta-Reichenau and gives several pharmaceutical preparations of this plant, a tincture, a wine, and two liquors.

Schimmel & Co.,[13] in 1894 distilled several kilos of oil from the freshly dried herb. The oil had a fine aromatic odor and taste and a blue color. The sp. gr. was 0.932. Cineol was identified in the lowest boiling fraction by means of Hirschsohn's iodol reaction.

ACHILLEA NOBILIS—As early as 1835 L. F. Bley[14] made a proximate analysis of the seeds, flowers, and the herb. By distillation with water he obtained from the seeds about 0.2 per cent of an oil which was almost colorless and of a thick butter-like consistency; the odor was penetrating, camphor-like; the taste strongly aromatic, and somewhat bitter; the sp. gr. was 0.970. From the flowers he obtained about 0.24 per cent of a slightly yellowish volatile oil having a powerful odor similar to that of the oil of *Achillea millefolium*, though finer, more camphoraceous, and aromatic; the taste was comphoraceous and somewhat bitter. The sp. gr. was 0.9830. From the herb there was obtained an oil having a slight yellow color, a penetrating, camphoraceous odor, and a strongly aromatic taste. In consistency it was almost like oil of rose. The sp. gr. was 0.970.

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[12] *Pharmaceutisches Handelsblatt*, 1880, No. 23.

[13] *Report of Sch. & Co.* Oct. 1894, p. 27.

[14] *Arch. d. Pharm.*, 51, pp. 69–80; *Ibid.*. 52, pp. 123–131; *Ibid.*, 53, 43–53 (1835).

As might have been expected with the small amount of oils at his disposal, Bley did not identify any of the chemical compounds present. No valuable addition was made to the chemical knowledge of this plant until 1905 when Echtermeyer investigated the oil of the flowering herb. The color of the oil was greenish-yellow, the odor comphoraceous, the taste bitter. $d_{15°}$ 0.9353; α_D 10.41°. The oil was fractionated. Borneol, camphene, acetic, formic, and capric acids were identified.

ACHILLEA CORONOPIFOLIA—Schimmel & Co., in 1893, obtained from Spain a deep blue, mobile volatile oil with a strong, pleasant odor somewhat similar to that of the oil of tansy. The sp. gr. at 15° was 0.9240. No analysis of the oil seems to have been made.

Other species of the genus *Achillea* which have been used medicinally are: *Achillea Ptarmica*, naturalized in the Eastern States; *Achillea nana* and *Achillea atrata* both natives of Europe. No chemical investigation of these species seems to have been made.

OBJECTS OF THE INVESTIGATION

This investigation of milfoil oil was undertaken for several reasons.

1. In connection with the cultivation of medicinal plants and the curing of fresh plant material to drugs, the selection of the best plant material for choice drugs naturally interferes with the economic utilization of the material harvested and hence with the desired commercial results, unless some satisfactory use can be found for the discarded portion. Yet the production of a choice drug should be a prime

consideration. Again, it is of greatest importance not to allow anything to go to waste.

In connection with alkaloidal medicinal plants and drugs the problem is relatively simple, for the inferior plant material can be utilized directly in the manufacture of pure alkaloids or of galenical preparations, the value of which can be established by assay. In connection with aromatic plants the problem is somewhat more complex for it is not only a quantitative but also a qualitative problem. In other words it is not merely a question as to whether so much oil can be obtained from the unsightly drug as from the more sightly or first class drugs, but whether the oil obtained from the lower two-thirds of a plant, *i. e.*, from the older leaves and stems, is to be considered qualitatively the equivalent of that from the upper third consisting of flowers, younger leaves, and but little stem. This question will have to be studied separately for each aromatic plant.

Inasmuch as milfoil is one of the plants which has been raised in the Medicinal Herb Garden by the government expert[15] for several years past and since choice drugs have been prepared from these plants, it seemed desirable to compare the oils obtained from the flowering tops such as are being used for the packing of standard drugs at the Station with that from the lower portions of the stem, and both with the oil obtained from the entire plant so far as it is ordinarily harvested for drug purposes. If the results of this investigation should prove that there is no valid objection to such practice, it would render possible the placing on the market of a choice drug, the distillation of the less desirable two-thirds of the plant as harvested, and the return of the bulk of the organic matter, after having been cooked, as it were, in the still, to the soil either in the form of mulching or compost.

2. Having once begun the investigation of the problem suggested under 1, it seemed desirable to extend the investigation to the oils obtained exclusively from the flowers, leaves, and stems respectively. The results of such an investigation would naturally admit of a more satisfactory interpretation of those obtained under 1.

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[15] See Annual reports to the Bureau of Plant Industry for 1909-1914 inclusive.

3. Milfoil oil being one of the few volatile oils that are intensely blue in color, it has long attracted attention because of its color which heretofore has been one of the chemical puzzles of the phyto-chemist. Inasmuch as Dr. Augspurger, of this laboratory, has observed that the blue color could be made to disappear by reducing the oil with palladium hydrogen, and since this seemed a very promising method of attacking this problem, it became very desirable to distill a larger amount of milfoil oil in order to secure sufficient material for investigation.

4. Having distilled one and two-tenths liters of oil, and having separated the blue oil by repeated careful fractionation, the opportunity to learn something more about the chemistry of this oil, of which so little is as yet known, was too good to be missed. Hence the detailed investigation of the oil was undertaken and carried out so far as the available material admitted.

5. While collecting the plant material for the oil distilled, attention was also given to a number of other questions of interest. Thus, the oil was distilled from the fresh material and from similar material after it had been dried and exposed for some days or weeks. The difference, if any, in the oil distilled from plants from high and dry ground from that distilled from low and wet ground but collected at the same time was also noted. Finally, the material being collected at different times of the season, the influence of the advance of the season and consequently the development of the plant was observed.

The results of this investigation so far as the problems outlined under 1, 2, 4, and 5 are concerned are herewith recorded. The blue fraction having been turned over to Dr. Augspurger, the report on this part will be made by him in the near future.

DISTILLATION AND DESCRIPTION OF THE OILS

During the summer of 1914 several samples of oil were obtained from milfoil collected near Madison and one sample (oil No. 12) from plants grown in the Station garden maintained as a cooperative experiment between the Department of Agriculture and The University of Wisconsin. All the oils obtained had a beautiful deep blue color and a peculiar camphoraceous odor.

Oil No. 1. The material from which this sample was obtained was collected July 9, when the flowers were in full bloom. These plants grew in rather low ground and were of good size, on the average not less than two feet high. The yield of oil was 0.164 per cent. The first portion of the oil which came over was colorless. For this oil two constants were determined: $d_{25°}$ 0.9020; $n_{D\ 19.6°}$ 1.4740.

Oil No. 2. In this case the material was collected July 13, partly in low ground and partly on high ground. On the average the plants were considerably smaller than those which furnished oil No. 1. The material was distilled the same day it was collected. Before beginning the distillation the condensing tube was washed with alcohol in order to remove any blue oil which might have remained from the first distillation. In this case, also, it was observed that a considerable portion of the oil which came over first was without color. The yield was 0.212 per cent. The following physical and chemical constants were determined: $d_{25°}$ 0.8930; $n_{D19.6°}$ 1.4718; acid number 1.09; saponification number 18.61; ester number 17.52, corresponding to 6.13 per cent. of ester calculated as bornyl acetate; saponification number after acetylating 56.73, corresponding to 11.48 per cent. free alcohol and 16.3 per cent. of total alcohol calculated as borneol.

When 5 c. c. of the oil were shaken in a cassia flask with a 4 per cent aqueous solution of potassium hydroxide, the diminution in the volume of the oil indicated the presence of 6 per cent by volume of phenol in the original oil.

Oil No. 3. The plants which furnished this oil were collected July 15 in rather low ground. The plants were all of good size, on the average about two feet high. Half of the material collected on this date was distilled the same day it was collected. The yield was 0.125 per cent; $d_{25°}$ 0.9035; $n_{D\ 19.6°}$ 1.4885.

Oil No. 4. This oil was obtained from the same lot of material which furnished oil No. 3, but in this case the material was allowed to dry at ordinary temperature until July

30 when it was distilled. The yield was 0.112 per cent; $d_{25°}$ 0.9080; $n_{D19.6°}$ 1.4880.

A comparison of the data obtained for oils Nos. 3 and 4 seems to indicate that the process of drying caused little or no change in the oil contained in the green plants.

Oil No. 5. The material which yielded this oil was collected on July 17 and was distilled the following day. These plants were similar in character to those which furnished oils Nos. 3 and 4, having been collected in the same locality. The yield was 0.123 per cent.

The following physical and chemical constants were obtained: $d_{25°}$ 0.9033; $n_{D19.6°}$ 1.4855; acid number 1.05; saponification number 25.4; ester number 24.35, corresponding to 8.52 per cent of ester calculated as bornyl acetate. A phenol assay made in the usual manner indicated the presence of 5 per cent by volume of phenol. An assay for cineol by the resorcinol method of Schimmel & Co., gave a diminution in the volume of the oil corresponding to 45 per cent of cineol. The identification of camphor and borneol, later, rendered this assay worthless since it is known that many oxygenated compounds besides cineol dissolve in 50 per cent resorcinol solution. An experiment in this direction showed that camphor and borneol both dissolve, camphor quite readily.

A test for aldehydes and ketones by heating with a 30 per cent neutral sodium sulphite solution indicated the presence of 2 p. c. of substances belonging to one or the other or to both of these classes of compounds.

Oil No. 6. The material for this oil was collected July 21 and was distilled on the following day. This oil and oil No. 5 were both obtained from plants collected in the same locality, and the plants were of about the same size and general appearance. The yield of oil was 0.111 per cent. Physical and chemical constants were obtained as follows: $d_{25°}$ 0.9098; $n_{D\,19.6°}$ 1.4890; acid number 1.35; saponification number 28.71; ester number 27.36, corresponding to 9.57 per cent of ester calculated as bornyl acetate; saponification number of the acetylated oil 71.36, corresponding to 13.2 per cent of free alcohol and 20.73 per cent of total alcohol calculated as borneol.

Oil No. 7. The material for this oil was collected July 23 and distilled the next day. The plants which furnished this oil grew on higher ground than did those used in experiment No. 6 and in a different locality. They were smaller and more mature. The yield was 0.21 per cent; $d_{25°}$ 0.8966; $n_{D19.6°}$ 1.4765.

Oil No. 8. In this case the plants were collected July 17. The weight of the undried material was 90 pounds. The flower heads were cut off and after drying for about two weeks were distilled alone. The weight of the air-dried flowers was 14.5 pounds. The amount of oil obtained was 56 gm. or 0.85 per cent calculated on the weight of the air-dried material. The first portion of the oil obtained was colorless but gradually became greenish and finally was deep blue as in all the other cases. As will be seen from the following data with the exception of the acid number there is no appreciable difference between this oil and the other oils all of which were obtained from the entire plants, roots excepted. $d_{25°}$ 0.9055; $n_{D\,19.6°}$ 1.4875; acid number 2.04; saponification number 28.65; ester number 26.61, corresponding to 9.31 per cent of ester expressed as bornyl acetate; saponification number after acetylation 69.77 corresponding to 12.93 per cent free alcohol and 20.25 per cent of total alcohol calculated as borneol.

When shaken with 50 per cent resorcinol solution about 50 per cent of the oil dissolved. When heated with 30 per cent solution of neutral sodium sulphite there was a diminution in volume indicating the presence of 2 per cent of aldehyde or ketone. Assayed for phenol by shaking with 4 per cent aqueous solution of potassium hydroxide the amount dissolved showed the presence of about 5 per cent of phenol. This included the free acid present.

Oil No. 9. The material used in this experiment consisted of the plants from which the flowers were removed in experiment No. 8. The weight of the air-dry material was 19.5 pounds. The yield of oil was 6 gm. or 0.067 per cent based upon the weight of the dried material. In this case, also, the first portion of the oil which came over was colorless; the oil then gradually became greenish and finally deep blue. The total weight of oil obtained in experiments Nos.

8 and 9 was 62 gm. or 0.15 per cent calculated on the total weight of undried material. The material was collected in the same locality as that which yielded oils 3, 4, 5, and 6. The only constant determined for the oil was the index of refraction. $n_{D\ 19.6^\circ}$ 1.4850.

Oil No. 10. One of the objects of these experiments in distillation was to learn whether the blue constituent of the oil is contained in other parts of the plant than the flowers. To obtain further knowledge on this point a small quantity of the large radical leaves was collected and distilled. The weight of the material before drying was 8.5 pounds. The material, air-dried, was distilled several weeks later. In this case the distillation was continued only two hours. In all other cases it was continued from three to four hours. Since the amount of oil obtained was very small the entire distillate was shaken out with petroleum ether and the condensing tube was washed with ether and the two solutions united. By evaporation of the solvent about 1.4 gm. of oil were obtained. The color was dark greenish-blue.

Oil No. 11. The flowers from 68 pounds of fresh plants collected August 14 were distilled October 7. The amount of oil obtained was 49 gm. The color of this oil, also, was deep blue. d_{25° 0.9087.

Oil No. 12. The plants used in this experiment were grown in the Station garden under the superintendence of G. A. Russell, the Government Expert of the Bureau of Plant Industry. About nine inches of the flowering tops were cut off and reserved for drug purposes. The remainder of the plants was distilled. The weight of the whole plants before drying was 117 pounds. The weight of the material distilled was about 15 pounds in the air-dried condition. The plants were collected June 15 and distilled about the middle of October. The amount of oil obtained was 11.4 gm. The color was deep blue.

Oil No. 13. In this experiment the material distilled was the portion which remained after cutting off the flowers from 68 pounds of undried material. The plants were collected Aug. 14, and were considerably dried up. All flowers and flower buds were carefully removed before distillation. The amount of oil obtained was smaller than that obtained in experiment No. 10, but as the color was blue the distillation furnished additional evidence that the blue substance is contained in other parts of the plant than the flowers.

Oil No. 14. This oil was obtained from material collected by Dr. L. F. Augspurger in Sheboygan County, at different times in July and August and was distilled in conjunction with him October 3. The specific gravity was the only constant determined. d_{25° 0.8926.

Oil No. 15. In order to learn if the blue constituent of oil of milfoil or the parent substance from which it may, possibly, result during the process of steam distillation is formed early in the life of the plant a small quantity of material was collected May 7-12, 1915, the plants varying from four to eight inches in height. 10.8 kilos of fresh material after drying a few days at ordinary temperature yielded 4.1 gm. of oil or about 0.038 per cent. Of this amount 1.5 gm. separated from the aqueous distillate and 2.6 gm. were obtained by extracting the distillate with ether. The portion of the oil which came over first was only slightly blue, but the entire product was of the same deep blue characteristic of all the other samples. It also possessed the same peculiar odor characteristic of the oils obtained from older plants.

For convenience in comparing these oils, their physical constants are herewith tabulated. Unless otherwise stated, the yield is based on the weight of the fresh material.

No.	Place of Collection	Condition	Yield	d_{25°	$^{n}D\ 19.6^\circ$
1	Sunset Point	dry	0.164 per cent	0.9020	1.4740
2	Highlands	fresh	0.212 per cent	0.8930	1.4718
3	Hammersley farm	fresh	0.125 per cent	0.9035	1.4885
4	Hammersley farm	dry	0.111 per cent	0.9080	1.4880
5	Hammersley farm	fresh	0.123 per cent	0.9033	1.4855
6	Hammersley farm	fresh*	0.111 per cent	0.9098	1.4890
7	Piper farm		0.213 per cent	0.8966	1.4765
8	Hammersley farm (flower, heads only)	dry	0.85 per cent	0.9055	1.4875
9	Hammersley farm (stems and leaves from No. 8)	dry	0.067 per ecnt		1.4850
10					
11				0.9087	
12	Med. Herb Garden	dry			
13					
14	Sheboygan Co	dry		0.8926	

It becomes apparent from this table that the yield of oil from the flowering plant, computed for fresh material, varied between 0.111 and 0.213 per cent. The slight differences in locality may be as much responsible as differences in season. It also becomes apparent that the two oils of this group showing the largest yield have the lowest densities (Nos. 2 and 7). With exception of No. 1, the index of refraction of these two oils is lower than that of the other five. It would seem, therefore, that some definite relation exists between yield on the one hand and density and refractive index on the other.

A comparison of the yield of oil from flower heads and that from the remaining leaves and stems shows that the bulk of the oil appears to be located in the inflorescence.

FRACTIONATION OF THE OIL

In order to reduce to a minimum the conditions which might bring about chemical changes in the blue constituent of the oil, the oil, without preliminary treatment of any kind, was fractionated under diminished pressure and the colorless fractions then successively treated in the manner necessary for the separation and identification of the various constituents. One liter of the oil was distilled under a pressure of 57 mm. until the temperature rose to 100°. The distillate measured 457 c. c. and was pale blue, though a small portion which came over first was colorless. The portion remaining in the flask was of a rather thick consistency and had a deep blue color. The volume of the residue was 530 c. c. The loss due to this distillation was 13 c. c.

The distillate first obtained was again distilled under the same pressure as before. The portion which came over between 72° and 80° was colorless and measured 264 c. c. The distillate which came over between 80° and 100° was pale blue and the residue in the flask was deep blue. The blue residue from the first distillation was again distilled under a pressure of 57 mm. and the process continued until the temperature reached 125°. Some of this distillate solidified in the condenser and receiver and by placing the higher boiling portion in a freezing mixture more of the solid separated and was filtered off. Beginning with the lowest boiling fraction all of the distillate was again fractionated under a pressure of 55 mm.

In the following table are given the boiling temperature, specific gravity, optical rotation in a 100 mm tube, the amount and color of each fraction. At the end of this distillation the total loss was about 30 c. c. most of which must have been drawn off through the pump.

Table No. 2

No. of fraction	t°(55 mm.)	$d\frac{25°}{15°}$	α_D	No. c. c.	Color
1	72– 80°	0.8535	–30.4	212	Colorless
2	80– 90°	0.8600	–22.5	125	Colorless
3	90–100°	0.8833	–14.1	81	Colorless
4	100–110°	0.9107	–16.7	70	Slightly yellow
5	110–120°	0.9360	–26.5	66	Slightly greenish
6	Blue residue	......	......	......	......

CHEMICAL EXAMINATION OF THE OIL

Removal of Acid and Examination of Phenol—In order to remove the free acid, all fractions were now shaken with a weak solution of sodium carbonate, and then washed with water till neutral, the washings being added to the sodium carbonate solution, which was reserved for further examination.

The fractions were then shaken with a 3 per cent aqueous solution of potassium hydroxide in order to remove phenol, then washed with water and the first washing from each fraction was added to the main alkaline solution. This alkaline solution was then shaken out with ether in order to remove dissolved or suspended oil and the ether layer removed. After acidifying the alkaline liquid with diluted sulphuric acid it was repeatedly shaken out with ether, the ether extracts united, dried with anhydrous sodium sulphate and the ether allowed to evaporate. There remained a small amount of a thick brown residue. Its taste was bitter but scarcely at all pungent. With alcoholic ferric chloride solution it gave a brown color tinged with purple. On the addition of water the whole mixture became decidedly purple. With an aqueous solution of ferric chloride, it gave a purple color at once. Salicylic acid, therefore, forms a part of this phenolic mixture.

TEST FOR ALDEHYDES—After the five fractions of the oil had been freed from acid and phenol they were tested with Schiff's reagent for aldehydes with the following results:

Fraction I gave a decided pink color in a few seconds.

Fraction II gave a very distinct pink color within one minute.

Fraction III gave very little color within two minutes.

Fraction IV gave quite a noticeable pink color within two minutes.

Fraction V gave more color than IV in the same time. Another fraction obtained by further distillation of the blue residue also gave considerable color within two minutes. These tests were repeated with all six fractions, the results agreeing perfectly with those first obtained. The fact that fraction I gave a pronounced reaction which diminished to almost nothing in fraction III, increased again in fraction IV, and became still more noticeable in fractions V and VI is a very strong indication of the presence of at least two aldehydes of different boiling points.

SEPARATION OF ALDEHYDES—All six fractions were next shaken out with an excess of a 40 per cent aqueous solution of sodium bisulphite and then washed with water until the wash water was neutral, the first wash water being added to the sodium bisulphite solution. After this treatment none of the fractions gave the test for aldehydes within two minutes.

Since there was evidence of the presence of two aldehydes in these fractions the sodium bisulphite solutions from the first three fractions were united, made alkaline with sodium carbonate, and subjected to steam distillation. The bisulphite solutions from the last three fractions were also united, made alkaline, and distilled with steam. From the first three fractions, and also from the last three, pleasant smelling turbid distillates were obtained which had entirely different odors. The first three suggested butyric aldehyde, the last three the odor of magnolia blossoms. Both distillates gave decided color reactions with Schiff's reagent and both gave precipitates with p-nitro phenyl hydrazine.

SAPONIFICATION OF THE FRACTIONS—After removal of free acid, phenol, and aldehydes, the five fractions thus far obtained were individually saponified by means of semi-normal alcoholic potassium hydroxide heating one hour on a boiling water bath. The alcohol was partly distilled from each fraction and the residual alkaline liquid in each case mixed with water, the oil separated, washed, dried with anhydrous sodium sulphate, and fractionally distilled twice under ordinary pressure. The boiling temperature, optical rotation, density, and volume of each fraction are given in the following table:

Table No. 3

No. of fraction	Boiling temperature	α_D	$d \frac{25^\circ}{15^\circ}$	No. of c. c.
I	below 160°	−33°	....	12
II	160°–163°	−32.3°	0.8530	57
III	163°–166°	−28.7°	0.8556	56
IV	166°–172°	−20.2°	0.8605	47
V	172°–180°	−10.9°	0.8710	44
VI	180°–186°	− 3.3°	0.8845	20
VII	186°–192°	+ 0.6°	0.8995	21
VIII	192°–200°	− 0.3°	0.9175	22
IX	200°–205°	− 6.3°	0.9260	28
X	205°–210°	− 7.8°	0.9345	20
Residue.				

HYDROCARBONS OBTAINED BY DISTILLING THE ALCOHOL FROM THE SAPONIFICATION MIXTURE—When the alcoholic distillates from the first three fractions were separately mixed with water a separation of oil took place. These oils were washed with water, dried, and distilled under ordinary pressure. The following fractions were obtained:

Table No. 4

No. of fraction	Boiling temperature	α_D	$d \frac{25^\circ}{15^\circ}$	No. of c. c.
I	155°–157°	−32.8°	....	7
II	157°–162°	−33.3°	0.8515	29
III	162°–163°	−25.5°	....	17
Residue.				

SEPARATION AND IDENTIFICATION OF CINEOL—In order to separate the cineol all fractions in table No. 3 were shaken with a 50 per cent aqueous solution of resorcinol. This treatment could not be expected to give pure cineol since other oxygenated compounds are present, namely camphor and borneol, both of which are quite soluble in a 50 per cent aqueous solution of resorcinol; this treatment, however, would yield the hydrocarbons in a purer state even if it did not remove the oxygenated compounds completely. Each fraction was first assayed by the resorcinol method by shaking 5 c. c. of the respective oil with 50 per cent aqueous resorcinol solution in a cassia flask. The amount of each fraction which dissolved was as follows:

Table No. 5

No. of fraction	Per cent dissolved	No. of fraction	Per cent dissolved
I	11	VI	58
II	13	VII	74
III	18	VIII	91
IV	26	IX	95
V	41	X	100

The entire amount of each fraction was then shaken twice with an excess of 50 per cent resorcinol solution, or until there appeared to be no further diminution in the volume of the fraction. The resorcinol layer, after standing long enough to become clear, was run off, the residual oil washed with water and the optical rotation again determined. That portion of the oil which had dissolved in the resorcinol solution was recovered as far as possible by subjecting the solution to steam distillation. In cases where the amount of oxygenated compounds recovered was very small that resulting from two or three fractions was mixed. In several cases, the amount of oxygenated compounds recovered by steam distillation of the resorcinol solution was smaller than the amount of oil which had dissolved when the fraction was shaken with the resorcinol solution. As none of the three oxygenated compounds known to be present would dissolve in the distillate sufficiently to account for the difference observed, it would seem that some constituent of the oil which had dissolved in the resorcinol solution had undergone a chemical change whereby it was rendered non-volatile with steam. Further examination will be necessary to settle this point.

Cineol being optically inactive its presence in a fraction would lower the rotation of that fraction, by mere dilution, and its removal would consequently raise the optical rotation. The actual results obtained in the first two or three fractions can be explained in this way, but the comparatively high rotation, namely, −16.06° for the mixture resulting from fractions V and VI can not be due to this cause. The removal of a mixture of oxygenated compounds having a dextro rotation as was the case with fractions from No. V upward, would, of course, increase the levo rotation of the residual oil but this levorotation could not be due to the presence of the borneol, which proved to be levorotatory, since it also must have been removed by the resorcinol solution. It is, therefore, extremely probable that the high levorotation of the residual oil from fractions V and VI is due to a hydrocarbon and there are strong indications that this hydrocarbon is limonene, a mixture of the dextro-and levo-limonene, the levo-form predominating. Besides, other facts also point to the presence of limonene.

By referring to table No. 6 it will be seen that the oxygenated portions separated from fractions V to IX inclusive are dextrorotatory. Now, both the camphor and the borneol separated from the oil were proved to be levorotatory; consequently in addition to the camphor and borneol there must have been some dextrorotatory oxygenated compound in those fractions.

Table No. 6

No. of fraction	Rotation of fraction before shaking with resorcinol sol.	Rotation after shaking with resorcinol sol.	Rotation of oxygenated portion recovered by steam distillation
I	−33°	−33.9°	
II	−32.3°	−33.9°	
III	−28.7°	−31.2°	
IV	−20.2°	−25.1°	
V	−10.9°		+5.1° (Sp. gr. at 25° 0.925°)
VI	− 3.3°	−16.06	+5.7°
VII	+ 0.6°	− 6.6°	
VIII	− 0.3°		+1.9°
IX	− 6.3°		

The effect produced on the optical rotation of each fraction by shaking with 50 per cent resorcinol solution is shown in the foregoing table, in which is also given the rotation, in a 100 mm. tube, of the oxygenated oil recovered from the resorcinol solution by steam distillation.

The amount of oxygenated compounds recovered from the first four fractions was small and the rotation was not determined. As the preliminary assay of fraction X showed that it dissolved completely in resorcinol solution, this fraction was not further treated.

The amount remaining undissolved when fractions Nos. VIII and IX were shaken with resorcinol solution was very small and the optical rotation was not determined.

IDENTIFICATION OF CINEOL

The odor of cineol is not observable in the original oil but in fraction V it is quite apparent, and in the oxygenated oil removed from this fraction by means of the resorcinol solution, it is still more apparent. A portion of fraction V was treated with iodol when there resulted the characteristic greenish-yellow crystals of cineol-iodol. These were washed with a little benzene and dried by pressing between filter paper. Although the melting point of this compound was somewhat low, namely 106°-107° instead of 111°-112° there is no doubt that cineol is present. The amount, however, is small, probably not exceeding 3 per cent.

IDENTIFICATION OF PINENE

A portion of fraction No. II, when treated in the usual way with ethyl nitrite, glacial acetic acid, and hydrochloric acid yielded a nitrosyl chloride having the m. p. 102°–103°. From this nitrosyl chloride a nitrol piperidide was prepared which showed the melting point 119°. As was to be expected from the rather high rotation of the fraction the preparation of the nitrosyl chloride was attended with some difficulty.

A nitrosyl chloride and a nitrolpiperidide were also prepared from fraction III.

Examination for Limonene

The portions remaining undissolved after treating fractions Nos. III, IV, and V with resorcinol solution were refractionated under ordinary pressure. Two small fractions boiling respectively at 165°–173° and 173°–180° were obtained. The specific gravity of the first fraction at 25° was 0.8470. For limonene there has been reported d_{20° 0.8460. For dipentene d_{20° 0.8440. Besides the close agreement in specific gravity both fractions had an odor suggestive of limonene. In order to obtain further proof of the presence of limonene an attempt was made to prepare from each of these fractions a nitrosyl chloride for the further purpose of preparing nitrolamines but in neither case was a nitrosyl chloride obtained. The boiling temperatures, the odor, and, especially, the specific gravity, though not positive proof of the presence of limonene, are, at any rate, strong indications of the presence of that hydrocarbon. The difference in rotation between the first and second fractions of terpene obtained from the alcohol distilled from the saponification mixtures makes it quite probable that there is a small quantity of a third hydrocarbon in the oil. If these fractions were composed of pinenes there could be no difference in rotation between them, provided, of course, that dextro-and levo α-pinene have the same boiling points.

Identification of Camphor

The white solid which first separated during the fractionation of the oil resembled camphor or borneol in odor and taste. Some of it was recrystallized from ligroin and, thus purified, was found to have the melting point 195°. The melting point of camphor is 175°–178.5° and that of borneol is 203°–204°. The melting point of this white solid indicated that it might be a mixture of camphor and borneol. In order to obtain proof of the presence of camphor some of the white solid was treated with hydroxylamine hydrochloride according to the method of Emil Fischer. Before the mixture was acidified it was shaken out with ether to remove some solid that was precipitated. The solid which was obtained on evaporation of the ether was crystallized from diluted alcohol. The melting point was 128°. The dilute alcoholic liquid from which this body crystallized yielded a further crop of crystals on standing. These were beautiful, fine, white needles with the appearance of being quite pure. The melting point was 126°. After acidifying the alkaline liquid with acetic acid, the mixture was again shaken out with ether. The solid obtained by evaporation of the ether was recrystallized from diluted alcohol. It melted at 118°. The melting point of camphor oxime is given at 117° to 119°. Further proof of the presence of camphor was obtained by the preparation of a semicarbazone. Some of the solid was treated with semicarbazide hydrochloride by the method of Zelinsky[16], for the preparation of semicarbazones from cyclic ketones. The solid which separated was first washed with ligroin to remove borneol. It was then crystallized from benzene. It was found to melt at 228°. It was again washed with ligroin and again crystallized from benzene when it had the melting point of 235°-236°. The melting point of camphor semicarbazone is given at 236°-238°. The low melting point of this compound was undoubtedly due to the presence of a trace of borneol. The presence of camphor is, therefore, established beyond doubt.

Identification of Borneol

Some of the white solid which has been proved to contain camphor was crystallized several times from ligroin and petroleum ether. A white crystalline solid was finally obtained which had the melting point 202°–203°. As the melting point of borneol is given at 203°–204° this substance must have been nearly pure borneol. To remove all doubt as to the identity of this substance some of the white solid which was supposed to contain borneol was heated with acetic anhydride and anhydrous sodium acetate. From this mixture there was obtained an oil which after being washed free from acetic acid had the odor of bornyl acetate. On cooling in a freezing mixture it crystallized. The crystals dried between filter paper had the melting point 29°.

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[16] *Ber.* 30. 1541 (1897).

This is the melting point given for bornyl acetate. Another portion of the white solid was mixed with a slight excess of phenyl isocyanate and allowed to stand several days. The solid which resulted was extracted with hot petroleum ether and filtered while hot. On cooling a mass of beautiful fine white silky needles separated. The melting point was 139°. According to Bertram and Walbaum[17] bornyl phenyl urethane melts at 138°-139°. Borneol is thus proved to be one of the constituents of the oil.

SEPARATION OF CAMPHOR AND BORNEOL

In order to separate the camphor and borneol, the white solid which has been proved to be a mixture of the two was first subjected to sublimation. The most volatile portion was found to have a melting point of 185°-186°. Some of that which volatilized last had a melting point of 199°-200°. As this method was very tedious it was decided to try the method of Haller[18], substituting phthalic acid anhydride for succinic acid. 12 gm. of the solid mixture were thoroughly mixed with an equal amount of phthalic acid anhydride and then heated in a sealed glass tube at 150° for forty-eight hours. The mixture was then treated with some excess of sodium carbonate and shaken out with ether to remove camphor. The ether was evaporated, the residue pressed between porous plates, and then sublimed. The melting point of the sublimate was 168°. In order to remove what appeared to be phthalic acid anhydride, the whole mass was triturated with a solution of sodium carbonate and then filtered. After having been dried, it was again sublimed. It was now found to melt at 178° and boil at 204°. The specific optical rotation in alcoholic solution was α_D –37.31°.

The aqueous solution containing the borneol in the form of acid bornyl phthalate was treated with sodium hydroxide and boiled to saponify the ester, and the borneol thus liberated and precipitated was filtered out. This was crystallized from petroleum ether. The melting point was 198°. After having been sublimed it melted at 203°. The specific optical rotation in alcoholic solution was α_D –36.14°.

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[17] *Arch. d. Pharm.*, 231, p. 303.

[18] *Compt. rend.*, 108, p. 1308 (1889).

FURTHER DISTILLATION OF THE BLUE RESIDUE

The blue residue was again subjected to further distillation under a pressure of about 15 mm. until the temperature rose to 145°. The distillate thus obtained was deep blue and rather thick. This distillate was again distilled under diminished pressure until the temperature rose to nearly 150°. The distillate was blue. By placing it in a freezing mixture about 9 grams of a white solid separated. The liquid filtered from this solid gave a very noticeable reaction with Schiff's reagent for aldehydes. In order to remove the aldehyde the whole liquid was shaken with an excess of a 40 per cent aqueous solution of sodium bisulphite and the oil separated and washed. It then gave almost no color with Schiff's reagent. The sodium bisulphite solution was examined, as already noted. This fraction of the oil freed from aldehyde was next saponified with alcoholic potassium hydroxide solution, the alcohol in part distilled off and the residue added to water. On standing over night a white solid separated. This was filtered off, washed, and dried between porous plates. The weight was 11.7 grams. The aqueous-alcoholic alkaline solution was shaken out with ether to remove unchanged dissolved oil. After removal of the ether, the liquid was acidified with diluted sulphuric acid and again shaken out with ether. After evaporation of this ether there remained a small amount of a reddish colored liquid having the penetrating odor of strong acetic acid together with a slight odor of valeric acid. This was made slightly alkaline with sodium carbonate and shaken out with ether to remove any phenol that might have been contained in this fraction of the oil. On evaporation of the ether only a very slight residue remained which was added to the phenol already obtained.

TREATMENT OF THE BLUE RESIDUE WITH FIFTY PER CENT RESORCINOL SOLUTION

In order to remove as completely as possible from the blue residue any oxygenated compounds which might still remain, the blue liquid which measured about 325 c. c. was shaken twice with a 50 per cent solution of resorcinol. Separation into two layers took place very slowly and several days standing was necessary before it was possible to remove the aqueous resorcinol solution. Very little of the blue oil dissolved. The solution was filtered through a dry filter paper to insure the removal of globules of oil. As thus obtained the solution was somewhat dark in color but green rather than blue. The filtered solution was then distilled with a current of steam. Only about 16 c. c. of oil came over. Unexpectedly its color was a deep blue, almost as blue as the original oil of milfoil.

IDENTIFICATION OF ACIDS

(A) THE FREE ACID REMOVED BY SHAKING WITH A SOLUTION OF SODIUM BICARBONATE.

The alkaline solution was evaporated to a small volume on a water bath, then made slightly acid with diluted sulphuric acid and the mixture distilled over a bare flame. The distillate was shaken out with ether and the ether allowed to evaporate spontaneously. A small amount of a slightly yellowish oily substance was obtained, which had the odor of butyric acid. This was dissolved in a small amount of sodium hydroxide solution in slight excess. Silver nitrate solution was then added to this drop by drop until no more silver oxide was formed, as indicated by the color of the precipitate. The silver oxide was filtered off and silver nitrate added to the filtrate in slight excess. The precipitate which at first was almost white was filtered off, washed, and dried when it was slightly brownish yellow. After further drying at 75°, the silver was estimated by ignition.

I. 0.1098 grams of the silver salt gave 0.0560 grams of silver corresponding to 51.18 per cent silver.

II. After further drying 0.1136 grams of the silver salt gave 0.0586 grams of silver corresponding to 51.58 per cent silver. Silver valerate contains 51.64 per cent of silver. These results would indicate that the acid was valeric acid although the odor was more like that of butyric acid. Of course it is possible that the product was a mixture.

(B) ACID FROM SAPONIFICATION OF THE FRACTIONS

The alkaline mixtures from the saponification of the five fractions of oil were united, shaken out with ether, concentrated on water bath, then acidified, and subjected to steam distillation. The distillate was collected in two fractions. From the first fraction a silver salt was obtained which upon ignition gave (1) 56.84 per cent of silver (2) 56.76 per cent of silver. In the preparation of the silver salt from the next fraction there was a very decided reduction, the product being very black and heavy. It is not known what caused the reduction. On ignition the substance yielded 91.5 per cent of silver.

(C) ACIDS OBTAINED FROM THE LAST FRACTION DISTILLED FROM THE BLUE RESIDUE

The alkaline mixture resulting from saponification of the highest boiling fraction was not mixed with the other alkaline saponification mixtures. After removal of the phenol the dilute sodium carbonate solution was acidified with diluted sulphuric acid and distilled over a direct flame. Two fractions were obtained, the first was neutralized with sodium hydroxide and then precipitated with silver nitrate. The first precipitate was dark even before drying. On ignition it yielded 72.66 per cent of silver.

The second precipitate was of a gray color and on ignition yielded 66.66 per cent of silver.

The third precipitate was also of a gray color and gave on ignition 66.11 per cent of silver.

Some of this fraction heated with alcohol and sulphuric acid gave the odor of ethyl acetate.

The second fraction was treated in the same manner as was the first. The silver salt obtained was grayish in color and upon ignition yielded 60.15 per cent of silver.

NON-VOLATILE ACIDS

The reddish brown mass which remained after distilling off the volatile acids from the acid mixture resulting from the saponification of the various fractions was mixed with barium carbonate, heated on a boiling water bath and filtered while hot, but on cooling only a slight sediment was formed. On the addition of silver nitrate a flocculent precipitate was formed, which by rapid filtering and washing was obtained nearly colorless. This was dried and the silver estimated by ignition. Ag = 36.18 per cent. Another sample prepared in the same manner but having considerably more color yielded 36.24 per cent of silver.

As will be seen by reference to the following table it is reasonably certain that oil of milfoil contains formic and acetic acids and at least one other, probably two others, namely, butyric and iso-valeric acids. The high result obtained in the case of formic acid was undoubtedly due to the reduction which took place.

In interpreting results such as those here given it must be borne in mind that mixtures of acids may be obtained of such a nature that the results might easily lead to erroneous conclusions.

Concerning the non-volatile acids present it can only be said that the data obtained furnishes little more than evidence that a non-volatile acid or a lactone is present.

Table No. 7

Theoretical percentage of silver in silver salts of fatty acids.	Percentage of silver found in silver salts of acids obtained from oil of milfoil.
Silver formate 70.58	72.66
Silver acetate 64.64	66.66
	66.11
	60.15
Silver butyrate 55.34	56.84; 56.76
Silver valerate 51.64	51.18; 51.58
Silver laurate 35.17	36.18; 36.24

SUMMARY

By this investigation of Achillea millefolium it has been shown;

(1) That a blue oil may be obtained from either the leaves or the flower heads; most of the oil being obtained from the latter.

(2) That it would not be profitable to distill the lower two-thirds of the plant.

(3) That the blue compound may be obtained from very young plants, though in very small amount.

(4) That drying the plant material apparently produces no change in either the quantity or the quality of the oil.

(5) That the oil contains the following:

l-α-pinene, d-α-pinene, l-limonene, l-borneol, bornyl acetate and other esters of borneol, l-camphor, cineol, salicylic acid, aldehydes, most probably two, formic acid, acetic acid, butyric acid (?), iso-valeric acid, at least one non-volatile acid or lactone and a blue constituent of high boiling point.

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A KEY FOR THE IDENTIFICATION OF ANIMAL PARASITES FOUND IN THE HUMAN FECES

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A KEY FOR THE IDENTIFICATION OF ANIMAL PARASITES FOUND IN THE HUMAN FECES

INTRODUCTION

Realizing the importance of accurate diagnosis of intestinal parasites for the scientific handling and specific treatment of disease, and being unable to find any organized literature which would lead to ready determination of a form found in the feces, we have attempted to arrange a key by means of which any animal parasite in the feces of man can be identified.

As the title implies, this is merely a key and is not intended as a complete treatise on the parasites found in the human feces. The primary object is identification, and the descriptions of the species have been greatly condensed, only those portions which are important as a means of differentiation and identification being given. A few forms which have been reported in man only a few times have not been included. For more detailed descriptions than are given here the reader is referred to any of the later textbooks on the subject.

The forms of animal parasites which may occur in the human feces are five in number: (1) eggs; (2) proglottids; (3) active protozoa or cysts; (4) nematodes (round worms); and (5) fly larvae. A knowledge on the part of the reader as to the general characteristics of such animals is assumed.

By way of explanation, let us cite a specific example as the most concrete and simplest method of explaining the use of the key. The consecutive numbers in the left margin refer to the sentences immediately following. The numbers in the left margin which are in parentheses refer to the alternate of the particular number with which each is associated; thus, 1 (48) indicates that 48 is the alternate of 1, and vice versa. The numbers in the right margin are merely guides in proceeding farther. Thus the first sentence reads as follows: "1 (48) Specimen is an egg................2." 1 goes with "Specimen is an egg." (48) is the alternate of 1 when (see key) the "Specimen is not an egg." In case the specimen is an egg, the "2" in the right margin tells the reader where to proceed.

As a concrete example, let us take a tapeworm proglottid which is longer than it is broad, and has a uterus which is median with 7–10 lateral, ramified branches. Starting at the beginning of the key we immediately pass to 48, since the specimen is not an egg. 48 refers us to 49 (70), which says that the specimen is a proglottid and passes us on to: "50 (61) Proglottids longer than broad..................51." "51 (54) Uterus composed of tubes, etc." The uterus of our specimen is not composed of tubes, so we go to alternate of 51 which is "54 (51) Uterus not composed of tubes—median ....55". "55 (56) Etc............" does not fit our specimen so we go to the alternate: "56 (55) Uterus not branching, etc..........57". Passing on to 57 we find that characteristic and proceed to: "58 (59) Branches heavy; 7–10 in number..............*Taenia solium.*" A brief description of the proglottid of *T. solium* is then given. In this case, as with all of the proglottids described, the proglottid is ripe, such as is found in the feces.

A few of the terms used may need a word or two of explanation. By a *cyst* is meant the resting stage of an animal which is surrounded by a permanent wall. The *embryophore* of a tapeworm egg is the inner shell; it lies next to the embryo. The *great hooks* of fly larvae are found in connection with the mouth. The *oncosphere* is the stage in the development of the egg of a tapeworm at which it appears in the feces. By the *operculum* of an egg is meant a lid or cover. A *proglottid* is one of the segments of a tapeworm. A *spicule* is a small chitinous, needle-like structure present in many of the Nematodes. The *stigmal plates* referred to in the descriptions of the fly larvae are small plates, at anterior and posterior ends of the larvae, which are used in breathing.

KEY

1 (48) Specimen is an egg..2

2 (15) Eggs with opercula; oval or ellipsoidal..................3

3 (10) Eggs contain embryos; have undergone segmentation and varying degrees of development within egg shell...4

4 (9) Egg shell brown..5

5 (6) Operculum and side of shell flattened; embryo in exact center........................*Dicrocoelium lanceatum*

Egg ovoid in form, with operculum and one side of shell flattened. Embryo fully developed when egg is deposited; it occupies the exact center of the shell, an even space intervening between it and the shell. A mass of granular matter at one end surrounds head of embryo like a cap, more or less completely concealing it. Size: 38–45x22–30 Micra.

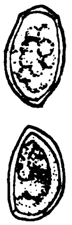


Fig. 1

Fig. 1. *Dicrocoelium lanceatum*, eggs.

6 (5) Operculum and side of shell not flattened..............7

7 (8) Eggs regularly oval; three distinct remnants of yolk; also yolk granules......*Clonorchis sinensis*

Egg unusually small, 29x16 micra, and assumes a dark brown or olive color in uterus of fluke; embryo already formed when egg is deposited; three distinct remnants of yolk in addition to granules seen in interior. Embryo can be forced out by sharp tap on cover glass; it is elongated in shape and 25 micra in length, tapering slightly towards posterior end; indication of head papillae often present.

Habitat: man only.

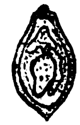


Fig. 2

Fig. 2. *Clonorchis sinensis*, eggs.

8 (7) Eggs narrowed at anterior end; high operculum .... *Opisthorchis felineus.*

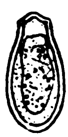


Fig. 3

Description. Egg oval with sharply marked operculum at pointed end; contains embryo in which cleavage is well advanced. Size: 30x11 micra. Habitat: Gall bladder and gall ducts of domestic cat; occasionally found in dogs; common as human parasite in Siberia.

Fig. 3. *Opisthorchis felineus,* egg.

9 (4) Egg shell transparent, embryo covered with cilia .... *Heterophyes heterophyes*

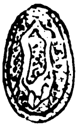


Fig. 4

Egg shell transparent and hyaline, oval and slightly pointed at opercular pole. Size 30x17 micra. Shell 1 micron thick with considerable strength; embryo formed before deposition of egg; it is elongated cylindrical with weakly marked projection at anterior end; large transparent spheres at posterior end 8 micra in diameter.

Fig 4. *Heterophyes heterophyes,* egg.

10 (3) Eggs without embryos but containing yolk substance 11

11 (12) Eggs oval with clear yellow-brown shell, broad at one end, tapering at other. Shell thicker at tapering end .... *Paragonimus westermanii*

Fully formed egg has oval clear yellow brown shell; shell relatively thin, broad at one end, tapering at the other; tapering end with thicker shell; broad end with small somewhat flattened operculum. Contents covered by thin membrane and in spaces between granular masses of yolk a clear viscous fluid is found. Size: 93.5x57 micra. Usual habitat is the lung.

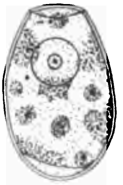


Fig. 5

Fig. 5. *Paragonimus westermanii,* egg.

12 (11) Eggs large with intense brown or yellow brown shell; contents difficult to distinguish .... (1) *Fasciola hepatica;* (2) *F. magna*

The eggs of these two forms are very similar, and can be very conveniently described in common. They are large and well formed, and when deposited have intense brown shells, making it difficult to distinguish the contents.

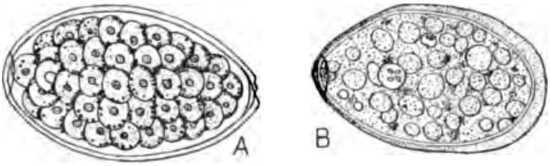


Fig. 6

Size: F. hepatica, .135–.145 mm.; F. magna, .142 mm. in length.

Fig. 6. A. *Egg of Fasciola hepatica;* B. *Egg of Fasciola magna.*

13 (14) Eggs oval with large oil globules, and mass of cleavage cells. 63x48–50 micra..*Diplogonoporus grandis*

Eggs from uterus have thick deep brown shell; general form oval; contents of shell consist of oil globules and mass of cleavage cells. Diameter of oil operculum: 20 micra. See also under 64.

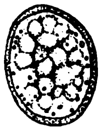


Fig. 7

Fig. 7. *Diplogonoporus grandis,* egg.

14 (13) Eggs oval; no oil globules or cleavage cells; large amount of yolk substance present. 68–71x45–50 micra....................................*Dibothriocephalus latus*

Eggs have thick brown shell; the lid becomes especially distinct at close of development. Large amount of yolk. Development carried out in water and not in maternal body. Inconspicuous egg cell usually almost completely concealed in mass of yolk cells. See also under 68.

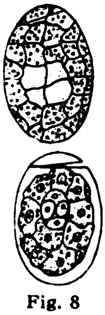


Fig. 8

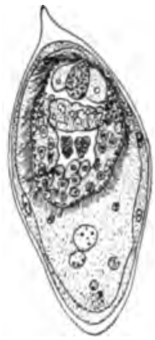
Fig. 8. *Dibothriocephalus latus,* eggs.

15 (2) Eggs without opercula oval or round....16

16 (45) Eggs have undergone segmentation and developed into embryos within shells.................................17

17 (20) Shell thin with single spine. Eggs bluntly spindle shaped or oval. 110–162x46–70 micra...............18

18 (19) Spine terminal, occasionally absent; egg present in urine, rarely in feces......*Schistosoma hematobium*

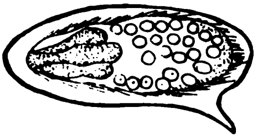


Eggs bluntly spindle shaped, yellowish in color, slightly transparent with thin shell provided with terminal spine (sometimes absent) at posterior pole. When voided in urine contains well developed embryo (sometimes dead and calcified). Eggs will not hatch in urine—only in water. The eggs are sometimes found in feces. Size 110–120x46–50 micra.

Fig. 9

Fig. 9. *Schistosoma hematobium*, egg.

19 (18) Spine lateral; eggs oval, found only in feces. 112–162x60–70 micra in size.... ....*Schistosoma mansoni*



Details of egg similar to S. hematobium.

Fig. 10

Fig. 10. *Schistosoma mansoni*, egg.

20 (17) Shell without spine; egg oval to round...............21

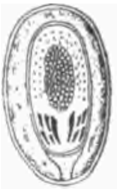


Fig. 11

21 (22) Eggs with 3 shells; external measurements, 80–100 micra long.. ....*Gigantorhynchus gigas*

Fig. 11. *Gigantorhynchus gigas*, egg.

22 (21) Eggs with less than 3 shells 23

23 (28) Eggs with thick, radially striated inner shell (embryophore); embryo with 6 hooks........................24

24 (25) Embryophore oval to round; size 39x33 micra—Africa...*Taenia africana**

Eggs with thick shells formed of radially striated membrane which appears finely granulated on exterior surface. Six hooks on onchosphere very distinct and measuring 7.8 micra in length. Found only in Africa. See also under 60.

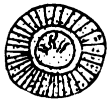


Fig. 12

Fig. 12. *Taenia africana,* egg.

25 (24) Embryophore oval, whitish to yellow, size 39x30 micra. America.............................*Taenia confusa**

Eggs oval in ripe proglottids; thin transparent external membrane; appearance of contents of embryophore varies in different specimens. Some have dark cap-like structures at one end, others at both ends, while the entire center is usually dark. To date this worm has only been found in Lincoln, Nebraska, U. S. A. See also under 55.

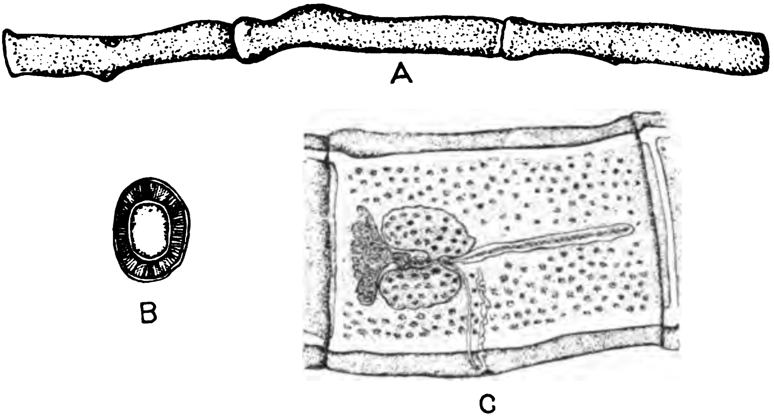


Fig. 13

Fig. 13. *Taenia confusa.* A, ripe proglottids, natural size; B, egg; C, proglottid.

26 (27) Embryophore ovoid; rusty brown; cosmopolitan and common.................................*Taenia saginata.**

Eggs sometimes retain outside covering consisting of thin yolk membrane drawn out at opposite poles into long delicate filaments. This membrane, however, usually absent in specimens found in feces. Eggs just formed in uterus are oval with polar projections constant. Embryophore thick and clearly striated. Size: 30–40x20–30 micra. Embryo 20 micra in diameter. See also under 59.

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* It is impossible to make a positive diagnosis of these parasites from the study of the eggs alone. The proglottids should be obtained and identification made from them. See 55, 58, 59 and 60.

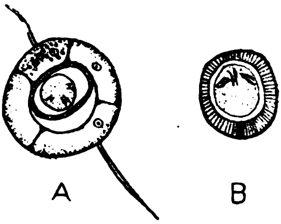

Fig. 14

Fig. 14. *Taenia saginata.* A, mature egg with external membrane; B, same, without external membrane.

27 (26) Embryophore nearly round; brown. Size: 31–38 micra in diameter............................*Taenia solium**
Eggs of T. solium resemble those of T. saginata (without original shell) very closely; see also under 58.

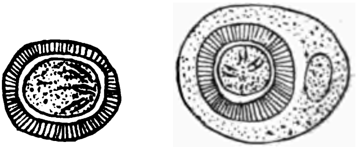

Fig. 15

Fig. 15. *Taenia solium,* eggs.

28 (23) Eggs with thin membranous inner shell (embryophore)..29

29 (32) Eggs in capsules.....................30

30 (31) 8–20 eggs in capsule, egg spherical; size 43–50 micra in diameter.. ....*Dipylidium caninum*

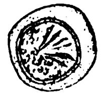

Fig. 16

Fig. 16. *Dipylidium caninum,* egg.

31 (30) 1–3 eggs in capsule with calcareous corpuscles; egg oval with 2 shells and 2 mammillate projections; onchosphere 8x15 micra..*Davainea madagascariensis*
See also under 52.

32 (29) Eggs not in capsules..33

33 (36) Embryo with hooks; eggs oval to spherical; 2 distinct membranes..34

34 (35) Filiform projection at each end of inner membrane..*Hymenolepsis nana*
Eggs usually spherical, oval ones rarely present, outer membrane delicate and irregular; inner regular and sharply doubly contoured with indistinct attachments at opposite poles from which a filiform appendage projects that is 3–4 times as long as egg. Both filaments lie rolled up between the 2 egg membranes and may simulate a third middle membrane. Size: external membrane 39 micra; internal membrane 28 micra in diameter. Hooks of onchosphere 9.2 micra long. See also under 62.

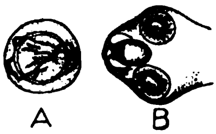

Fig. 17

Fig. 17. *Hymenolepsis nana*, egg.

35 (34) No filiform projections at one end of inner membrane; outer membrane yellow; may be radially striated................................*Hymenolepsis diminuta*
Eggs oval to round; external membrane yellow, delicate and may be indistinctly striated. Internal membrane has 2 polar knobs, but no filaments are attached to it; onchosphere elliptical; size 36x28 micra. Hooks 11 micra long. See also under 66.

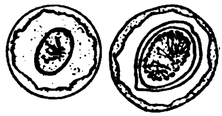

Fig. 18

Fig. 18. *Hymenolepsis diminuta*, eggs.

36 (33) Embryo without hooks; eggs oval.......................37

37 (44) Shell thin and smooth..38

38 (39) Shell flattened near one end; size 50x16–20 micra; contains well formed embryo when deposited................ ...*Oxyuris vermicularis* (pin worm)

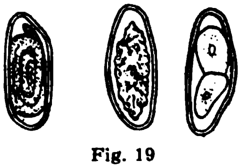

Fig. 19

Fig. 19. *Oxyuris vermicularis*, eggs.

39 (38) Shell regularly oval with broad rounded poles; colorless or clear yellow..40

40 (43) Contents of shell consist of dark granular mass in various stages of cleavage from few celled stage to partially formed embryo, and separated from shell by large clear space; shell colorless.....................41

41 (42) Regularly present during infection......................
..........*Agchylostoma duodenale, Necator americanus*

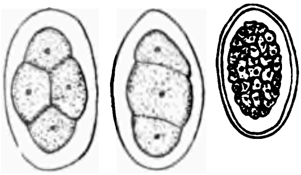

Fig. 20

The eggs of these two forms differ mainly in size; A. duodenale measuring 50x23–27 micra, and N. americanus 57–83x35–52.5 micra, and positive identification is made from the parasite itself. See also under 90 and 91.

Fig. 20. *A. duodenale* and *N. americanus*, eggs.

42 (41) Eggs present in feces only during attacks of diarrhoea; shell clear yellow.................................
............................*Strongyloides stercoralis*

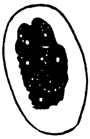

Fig. 21

Eggs elliptical with thin clear yellow shell; contents granular, distinctly in cleavage and separate from shell by clear space. Size: 50–58x30–34 micra.

Fig. 21. *Strongyloides stercoralis*, eggs.

43 (40) Contents form solid morula-like mass, separated at either end from shell by small clear space..........
....*Strongylus subtilis*

Eggs are oval with very thin shell. Contents strongly granular and split into numerous cleavage spheres 5–10 micra in diameter, forming a solid morula-like mass. A narrow unoccupied space at both ends separates this mass from the thin hyaline shell. Size 72–80x40–43 micra.

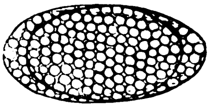

Fig. 22

Fig. 22. *Strongylus subtilis*, egg.

44 (37) Shell thick with numerous depressions..*Dioctophyme renale*

Rare; eggs oval with thick brown shell with numerous depressions. Size 68–80x 40–43 micra.

Fig. 23. *Dioctophyme renale*, eggs. A, surface view; B, optical section.

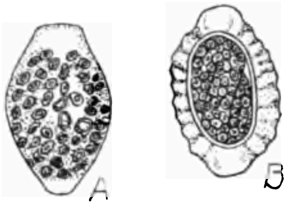

Fig. 23

45 (16) No embryo, eggs have not undergone segmentation..46

46 (47) Shell heavy, brown and perforated at both poles; orifices closed by transparent plugs; ellipsoidal. Size 50–54x23 micra...................*Trichuris trichiura*

Synonyms: *Trichocephalus hominis; Trichocephalus dispar.*

Fig. 24. *Trichuris trichiura*, eggs.

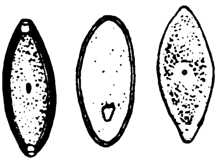

Fig. 24

47 (46) Shell thick and transparent with rough mammillated external coat of albumen (stained brown by feces) no perforations, elliptical to round..*Ascaris lumbricoides*

Many variations which may confuse. *Normal fertilized egg* is round to elliptical, 3 fold thick shell, with mammillated albuminous covering of yellowish tone; contents finely granular and round in form. Thus between content and elongated shell is seen a crescentic space at each end which is filled with a clear fluid. Nucleus may appear as clear mass in center of spherical mass. *Unfertilized egg* is oval or elliptical with irregular contour and occasionally with lateral curvature

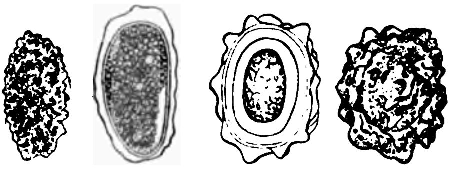

Fig. 25

of shell. Numerous variations apparently due to resisting power of shell and irregular distribution of albuminous covering. Shell proper doubly contoured, relatively thin, and with less distinct internal boundary. Contents consist of large refractive bodies filling entire space, leaving no evidence of crescentic clear area near poles as in fertilized egg. Eggs vary as to size.

Fig. 25. *Ascaris lumbricoides*, eggs.

48 (1) Specimen not an egg..49

49 (70) Specimen a proglottid..50

50 (61) Proglottid longer than broad..51

51 (54) Uterus composed of tubes, which lose their walls on becoming mature, allowing eggs to lie free in parenchyma..52

52 (53) Proglottid contains 300–400 such eggs..*Davainea madagascariensis*

Proglottid 2.0 mm. long x 1.4 mm. wide. Genital pore unilateral near proximal corner. Testes number about 50; long vas deferens and fusiform cirrus pouch. Receptaculum seminis long and broad. Uterus composed of number of tubes rolled up on each side into almost spherical coil. Windings uncoil when mature, filling proglottid's lose walls leaving eggs free in parenchyma surrounded by capsule.

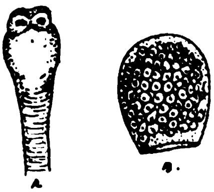

Fig. 26

Fig. 26. *Davainea madagascariensis*. A, scolex; B, free ripe proglottid.

53 (52) Proglottid contains 60–70 egg follicles..*Davainea asiatica*

Genital pore unilateral. Testes globular, cirrus pouch pyriform; female organs anteriorly. Uterus breaks into 60–70 large egg follicles.

54 (51) Uterus not composed of tubes; median..55

55 (56) Uterus with 14–18 short dichotomous branches..*Taenia confusa*

Mature proglottid 27–35 mm. x 3.5–5.0 mm. Genital pore irregularly behind middle of lateral border. Testes numerous; vas deferens not much coiled; cirrus pouch thick walled, cirrus with hairs; receptaculum seminis globular; ovary small and double, bean shaped; uterus median with 14–18 short dichotomous branches. For proglottid see figure 13.

56 (55) Uterus not branching dichotomously..................57

57 (60) Uterus with lateral ramified branches................58

58 (59) Branches heavy, 7–10 in number....................*Taenia solium*
Mature proglottid 10–12 mm. long x 5–6 mm. broad. Genital pore lateral and irregularly alternate. Uterus with 7–10 ramified lateral branches, 3 ovaries, the third formed by subdivision of one on side of genital pore.
Fig. 27. *Taenia solium*, proglottid.

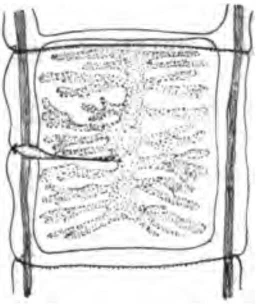
Fig. 27

59 (58) Branches more delicate; 20–35 in number..*Taenia saginata*
Mature proglottid 16–20 mm. long x 4.7 mm. broad. Genital pore irregularly at sides. Uterus median with 20–35 ramified lateral branches.
Fig. 28. *Taenia saginata*, A, ripe; B, immature.

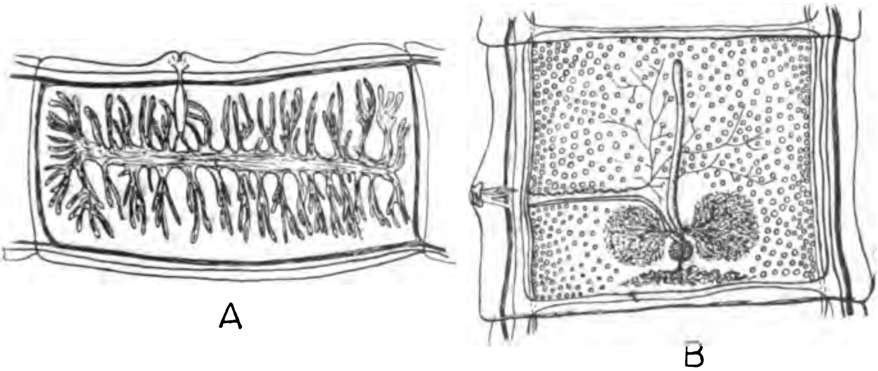

Fig. 28

60 (57) Uterus with 15–24 lateral non-ramified branches .... *Taenia africana*
Mature proglottids longer than broad. Measurements vary. Genital pore irregularly alternate on lateral margin. Testes very numerous, vas deferens very convoluted with thick pear shaped cirrus pouch, vagina and cirrus beset with bristles. Receptaculum seminis large; ovary large and double; vitelline gland at posterior border, uterus median; 15–24 lateral non-ramified branches.

61 (50) Proglottid broader than long.................................62

62 (63) Proglottid less than 1 mm. wide................................ .... *Hymenolepis nana*
Proglottids very small (0.4–0.9 mm. wide x 0.014–0.030 mm. long). Genital pore marginal. Mature uterus fills entire segment. Contains 30 or more eggs. See figure 17B for proglottid.

63 (62) Proglottid more than 1.0 mm. wide.....................64

64 (65) Proglottid with 2 complete sets of genital organs .... *Diplogonoporus grandis*

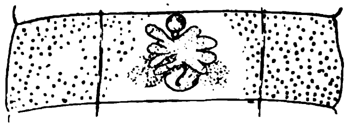

Fig. 29

Proglottids 1.5 mm. broad in front; 2.5 mm. broad behind; very short (0.45 mm.). Ventral grooves on either side of median line within which genital pores lie. Uterus makes only few loops.

65 (64) Proglottid with single set of genital organs........66

66 (67) Mature uterus fills entire proglottid. 3 testes in each segment........................ *Hymenolepis diminuta*
Anterior proglottids have yellow spot due to distended receptaculum seminis. Posterior proglottids brownish grey due to mature uterus. Genital pore on left side. .66 mm. long x 3.5 mm. wide.

67 (66) Uterus in center of proglottids. Many testes....68

68 (69) Uterus rosette-like................*Dibothriocephalus latus*
Proglottid very broad (10–20 mm.). Posterior lateral angles project. Testes numerous; yolk glands in pairs; shell gland behind; ovaries on each

side of median line behind. Uterus in form of rosette with 4–6 convolutions and own opening behind. 2 genital orifices.

Fig. 29. *Diobothriocephalus latus*, proglottid.

69 (68) Uterus with median stem and big dichotomous branches..*Taenia philippina*

Proglottid much broader than long, 4–5 mm. x 0.8–1.0 mm. Surface and margin extend posteriorly in elongated cuff-like projection over succeeding segment. Vagina without seminal vesicle. Genital pore irregular on lateral borders. Mature uterus very compact with median stem, and numous long dichotomous branches

70 (49) Specimen not a proglottid....................................71

71 (74) Specimen an amoeba..72

72 (73) Ectoplasm well defined during rest; encysted form with 4 nuclei..............*Löschia* (*Entamoeba*) *tetragena*

20–40 micra in diameter; spherical at rest; with cysts containing 4 nuclei; numerous red blood corpuscles—ectoplasm often visible as clear hyaline highly refractive layer, nucleus clearly visible with constant cyclic changes. Karyosome with 1 granule.

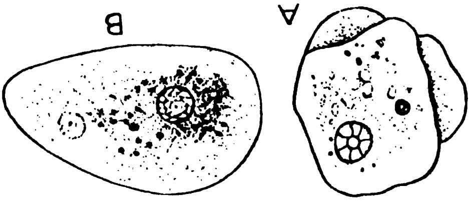

Fig. 30

Fig. 30. *Löschia tetragena*. A, vegetative form; B, same in motion.

73 (72) Ectoplasm not clearly distinguished during rest. Encysted forms with 8 nuclei....................................
....*Löschia* (*Entamoeba*) *coli*

Cysts contain 8 nuclei; almost always without red blood corpuscles. Ectoplasm invisible except when pseudopodia are protruded. Nucleus subcentral, Karyosome often with 2 granules. Cytoplasm vacuolated and contains bacteria.

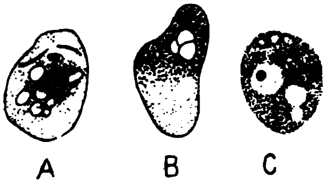

Fig. 31

Fig. 31. *Löschia coli.* A, vegetative; B, same in motion; C, cyst.

Note:—According to recent investigations, there are only 2 "good" species; i.e. *L. coli* and *L. tetragena.* The other intestinal amoeba described are supposedly forms of the above 2. For further information, see Castellani and Chalmers, "Manual of Tropical Medicine," 1913.

74 (71) Specimen not an amoeba........................ 75

75 (92) Specimen a nematode (round worm)........................ 76

76 (77) 15–40 cm. long........................ *Ascaris lumbricoides*

The living form is red or greyish yellow. Elongated spindle shape. 4 oral papillae. Male 15–25 cm. long. Posterior end conical and bent hooklike ventrally. Spicules 2 mm. long, curved, broadened at free end. Many (70–75) papillae around orifice of cloaca, 7 pairs of which are post anal. Testicular tube much folded and about 8 times the body length. Female 20–40 cm. long. Posterior end conical and straight. Vulva between anterior and middle third. Uterine tubes (2) pass straight to posterior end. Convoluted ovaries 10 times body length.

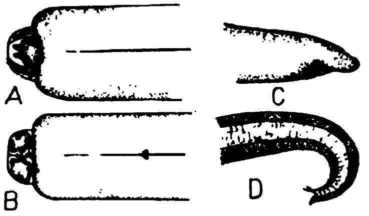

Fig. 32

Fig. 32. *Ascaris lumbricoides*, adult. A, dorsal view of anterior end; B, ventral view; C, posterior end of female; D, posterior end of male.

77 (76) Less than 15 cm. long..............................78

78 (85) Posterior end coiled..............................79

79 (80) Anterior end drawn into long whip-like process..*Trichuris trichiura* (female)

Female 40–45 mm. long; from anterior end body tapers back to whip-like process.

Fig. 33. *Trichuris trichiura*. Adult female.

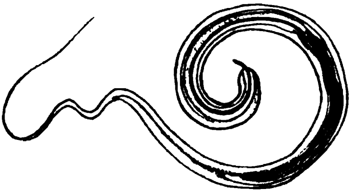

Fig. 33

80 (79) Anterior end blunt or rounded..............................81

81 (82) 2 spicules at posterior end of body..*Strongyloides stercoralis* (adult)

2.2 mm. long x 0.034 mm. wide, cuticle finely striated transversely, mouth surrounded by 4 lips. Oesophagus one-fourth length of body. Anus opens shortly in front of posterior end. Genital orifice in female in posterior third.

Fig. 36. *Strongyloides stercoralis*, adult.

82 (81) One spicule at posterior end of body..............................83

83 (84) Posterior extremity has 6 papillae..*Oxyuris vermicularis* (male)

White; 3 small retractile papillae around mouth; male 3–5 mm. long; posterior end rolled ventrally and has 6 papillae.

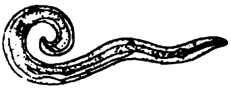

Fig. 35

Fig. 35. *Oxyuris vermicularis*, adult male.

84 (83) Posterior extremity without papillae. Spicules 2.5 mm. long..............................*T. trichiura* (male).

Male 40–45 mm. long; spicule 2.5 mm. long and lies in retractile pouch beset with spines.

85 (78) Posterior end not coiled..............................86

86 (89) Tail tapers to point.

87 (88) Oesophageal bulbs double. Length 1 mm..*Strongyloides stercoralis* (free living form)

Have pointed tails; 250 x 13 micra. Double oesophageal bulb. If temperature is low, develop into filariform embryos. If temperature is warm they develop into adult stercoralis.

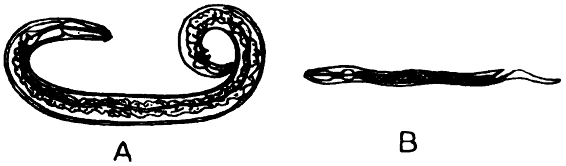

Fig. 36

Fig. 36. *Strongyloides stercoralis.* A, adult female; B, larva.

88 (87) Oesophageal bulb single. Length 10 mm...*Oxyuris vermicularis* (female)
Female 10 mm. long; anus about 2 mm. in front of tail tip; vulva in anterior third of body; tail not curled, but tapers to a point.

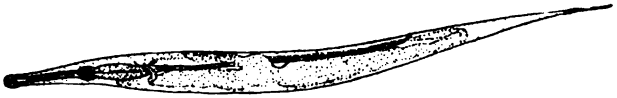

Fig. 37

Fig. 37. *Oxyuris vermicularis.* Female.

89 (86) Tail blunt or fan-shaped..90

90 (91) Oral cavity with 2 pairs of teeth ventrally and 1 pair dorsally............*Agchylostoma duodenale* (male)
Body cylindrical and tapering. Flesh colored during life. Cuticle ringed. Mouth terminal; chitinous wall which carried 2 pairs of hooked teeth ventrally and 1 pair dorsally. Head gland near ventral teeth and runs about one-half body

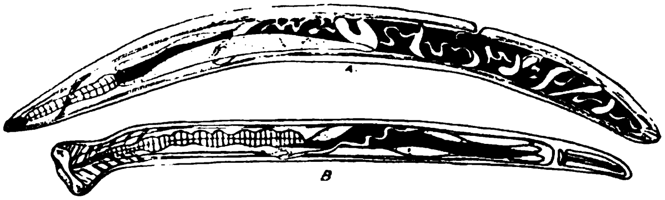

Fig. 38

length. Male 10 mm. long x 0.4–0.5 mm. wide; bursa copulatrix at posterior end supported by chitinous rods; 2 spicules project through opening of bursa about 2 mm. long, and can be retracted. Tubular testes, oval seminal sac, long cement gland. Female 12–13 mm. long; vulva at middle and posterior thirds from which short vagina opens into 2 tubes.

Fig. 38. *Agchylostoma duodenale.* A, female; B, male.

91 (90) Oral cavity without teeth but with ventral and dorsal chitinous plates................ *Necator americanus* Small mouth capsule armed only by semilunar plates. Head bent strongly dorsally. Bursa bilobed in male. Vulva in female in anterior part. Deep in mouth are 1 pair of ventral and 1 pair of dorsal lancets—head gland. Male 7–9 mm. long 0.3–0.35 mm. wide; spicules long and slender and end in barbed points. Female 9–12.6 mm. long.

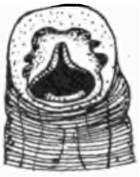

Fig. 39

Fig. 39. *Necator americanus.* Head.

92 (75) Specimen a fly larva...93

93 (94) Body with lateral and dorsal spinous processes..... .... *Homalomyia*

Fig. 40. *Faumia scolaris.* Larva. Flat, fusiform, each segment has long bristly processes. Mouth parts obscure; stigmal plates dorsally on last segment. Pair of spinous processes dorsally on each segment forming 2 rows. Row of these on upper and lower side of body, making 6 rows. Pair of anterior processes on head. Body surface scabrous. Each ventral segment transversely divided by narrow line terminating on each side in small tubule.

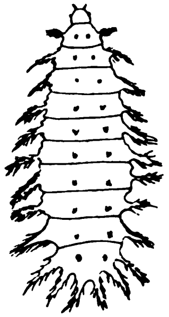

Fig. 40

94 (93) Body without lateral and dorsal spinous processes 95

95 (98) Body ending in 2 fleshy processes........................96

96 (97) Processes bearing stigmal plates; body about 5 mm. long...*Drosophilia*

Body slender in front; distinct papillae on head. Anterior spiracles obscure with 8–10 long branches. Each body segment slightly constricted in middle, basal area roughened; anal tubercle broad, dark, bilobed, and not very prominent; around tip of body are several pairs of tubercles; stigmal plates on tips of 2 cylindrical processes resting on elevation at tip of body. Common in over-ripe fruit, jellies, jams, vinegar, pickles, etc.

97 (96) Processes not bearing stigmal plates. Body 10 or more mm. long..................................*Piophilia-casei*

Head emarginated from above, each corner projecting in a papilla. Two well separated hooks. Anterior spiracles have 10 lobes. From 6th segment on, have raised area on base provided with small teeth. Last segment has outer angle prominent on each side near base. Each main tracheal tube black for short distance beyond tip. Occurs in cheese, ham, etc.

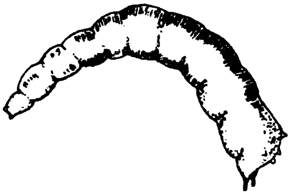

Fig. 41

Fig. 41. *Piophilia casei.* Larva.

98 (95) Body truncated or broadly rounded at end........99

99 (100) With 1 great hook. Posterior stigmal plates with winding slits..*Muscina*

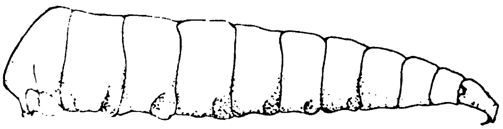

Fig. 42

But 1 great hook; posterior stigmal plates have 3 sinous slits, characters not found in allied forms. Anterior part of body more slender than Sarcophaga. Spinous parts of segments confined to ventral surface. Anal tubercles smooth, no prominent outlines to stigmal field. Prothoracic spiracles have only a few lobes.

Fig. 42. *Musca domestica.* Larva.

100 (99) Two great hooks, no buttons to stigmal plates.. *Sarcophagidae*

Two anterior hooks, posterior stigmal plates have three straight slits which are subparallel and not confluent. Stigmal plates depressed and form pit.

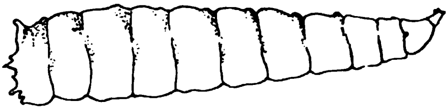

Fig. 43

Body segments bear complete rings of spinose areas and often supplementary pads on the sides. These larvae prefer animal matter and are found in cheese, oleomargarine, herring, dead insects, human feces.

Fig. 43. *Sarcophaga* sp. Larva.

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